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MEDICAL SUBJECT HEADINGS

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This highlights-index for the year 2001 changes *Practical Pointers* from a throw-away to a reference. It contains about 130 Medical Subject Headings (MESH) which are linked to the highlights of related abstracts. Some subject headings contain highlights of over 10 articles; some only one or two.

The highlights in turn are linked to the original abstract indicated by number. For example, 7-12 indicates the 12th abstract in sequence for July; 3-4 the 4th abstract in sequence for March.

This annual summary will allow interested readers to rapidly review and remember interesting and clinically relevant articles selected during the year as being of practical importance to primary care adult medicine.

The entire content of this section of *Practical Pointers* can be read in a few hours.

In the web form (www.practicalpointers.org) automatic links (html) are provided. On the web, issues for 1999, 2000 are already available. The complete 2001 issues will soon be available.

Monthly issues as an attachment to e-mail will be sent on a timely basis to anyone interested. Just send me your e-mail address.

Thank all for your support and interest.

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CORONARY HEART DISEASE
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PROFESSIONALISM
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VASCULAR DEMENTIA
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VITAMINS

WEBSITES

WHITE COAT HYPERTENSION (See HYPERTENSION)

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ACUTE CORONARY SYNDROME

4-4 RESULTS OF CURE TRIAL FOR ACUTE CORONARY SYNDROME

Clopidogrel (*Plavix*— an antiplatelet drug), acts to inhibit adenosine diphosphate, an activator of platelet aggregation.

This randomized, double-blind trial entered over 12 500 patients with acute coronary syndromes. For every 1000 persons treated for 9 months, an estimated 28 cardiovascular deaths, MIs, or strokes would be prevented.

Practical point: The treatment of acute coronary events, including myocardial infarction, is in a state of flux. Use of thrombolysis is giving way to use of platelet inhibitors and early coronary revascularization. Primary care clinicians should be able to identify patients with acute coronary syndromes and begin treatment as early as possible. They should correlate the best current treatment with their cardiologist consultants. Watch for evolving developments.

4-7 EFFECTS OF ATORVASTATIN ON EARLY RECURRENT ISCHEMIC EVENTS IN ACUTE CORONARY SYNDROMES: The MIRACL Study

High dose atorvastatin started within 1 to 3 days after presentation for acute coronary syndromes was associated with a reduction in risk of early recurrent ischemic events, but with no other significant clinical benefit.

Practical point: Statin drugs given immediately after onset of acute myocardial infarction or unstable angina may be associated with only small benefits over 4 months. Nevertheless, statins should be started for secondary prevention and maintained over years. Starting early in the hospital will encourage compliance.

6-2 OPTIMAL TREATMENT OF ACUTE CORONARY SYNDROMES — An Evolving Strategy

This article summarizes the latest recommendations. A reference algorithm is presented on p 1941.

Practical point: Primary care clinicians can serve their patients optimally by immediately beginning non-interventional measures (aspirin, heparin, oral beta-blocker, and medication for pain control). Primary care clinicians remote from emergency centers must keep up with the rapid changes in therapy in order to correlate urgent treatment with their cardiologist colleagues. Each minute of myocardial ischemia adds to risk. The new bolus agents will facilitate early fibrinolysis out of hospital.

8-6 EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

The anti-platelet agent clopidogrel (*Plavix*) given in addition to aspirin, had significant benefits in patients with acute coronary syndromes without ST elevation. The risk of major bleeding was increased.

Practical point: Primary care clinicians and their patients should consider the benefit/harm/cost ratio of clopidogrel. Harms are significant, costs high. but benefits may be life saving. The stakes are high.

10-14 THE PROGNOSTIC VALUE OF B-TYPE NATRIURETIC PEPTIDE IN PATIENTS WITH ACUTE CORONARY SYNDROMES.

A single measurement of BNP obtained within a few days of onset of ischemic symptoms provided powerful risk-stratification information across the entire spectrum of acute coronary syndromes.

It predicted long term risk of death and non-fatal coronary events. The prognostic usefulness persisted after adjustment for the presence of HF and other important predictors of mortality.

The authors suggest — B-type natriuretic peptide should be measured after an acute coronary syndrome in order to identify the risk of adverse outcomes. Treatment should be adjusted accordingly.

Practical point: Primary care clinicians should keep this marker in mind. It has not yet reached frequent clinical application, but probably will in the near future.

10-15 ACUTE CORONARY SYNDROMES — BEYOND MYOCYTE NECROSIS

Tests for neurohumoral activation (elevated brain natriuretic peptide) and inflammation (C reactive protein) may augment our ability to identify patients at risk of adverse events, and potentially help to reserve the most expensive and aggressive therapies to individuals at highest risk.

Practical point: These two proteins will be increasingly used as risk markers.

AIR TRAVEL

9-18 SEVERE PULMONARY EMBOLISM ASSOCIATED WITH AIR TRAVEL

The greater the distance and time traveled in airflights the greater the risk. The absolute incidence is low.

Almost all patients had high and moderate risk of thromboembolic disease.

The sitting position is associated with venous stasis. The double 90-degree angle bends at the knee and hip impede flow.

Practical point: Simple behavioral and mechanical prophylaxis should be considered to prevent air-travel associated PE and DVT, especially in patients with risk factors.

ALBUMINURIA

7-3 ALBUMINURIA AND RISK OF CARDIOVASCULAR EVENTS, DEATH, AND HEART FAILURE IN DIABETIC AND NON-DIABETIC INDIVIDUALS.

Any degree of albuminuria is a robust, independent risk factor for future cardiovascular events in individuals without DM who have increased risk factors for CVD, as well as those with DM. The risk increases as the albumin/creatinine ratio increases, starting well below the cutoff for microalbuminuria.

Practical point: Primary care clinicians should screen for albuminuria (both dipstick positive and below) in diabetic patients and high risk patients without diabetes. It is an inexpensive and rewarding prognostic indicator which calls for early intervention.

ALCOHOL

4-5 PRIOR ALCOHOL CONSUMPTION AND MORTALITY FOLLOWING MYOCARDIAL INFARCTION

Moderate alcohol consumption in the year prior to an acute MI was associated with reduced mortality following infarction.

Practical point: What should we advise abstainers when discharged from the hospital following an acute MI? The number needed to treat (among those using alcohol in the year prior to the MI) to benefit one patient is comparable to other pharmacotherapeutic interventions. I believe some competent stable patients and their families should be informed of the likely (but not proven) benefits of one drink a day.

They may then choose for themselves. Just as for any drug, a prescription for "A cocktail before dinner (1 oz spirits), or a glass of wine (4 oz) with dinner — not both" may be written. Individuals who do drink moderately and develop left ventricular dysfunction, heart failure, or other effects of CHD generally should *not* be told to discontinue consumption.

4-6 MODERATE ALCOHOL CONSUMPTION AND RISK OF HEART FAILURE AMONG OLDER PERSONS.

Moderate alcohol consumption was associated with lower risk of heart failure among older persons. The observed benefits may not be entirely mediated by a reduction in risk of MI.

Practical point: Primary care clinicians must consider the consistently substantial benefits of alcohol reported by epidemiological studies. Advice must be individualized. Stable individuals who consume small amounts of alcohol daily should not be told to stop. Abstinent individuals may be told of the risks and benefits and a prescription for "one drink daily" may be considered.

ALLERGIC RHINITIS

12-4 SUPERIORITY OF AN INTRANASAL CORTICOSTEROID COMPARED WITH AN ORAL ANTIHISTAMINE IN THE AS-NEEDED TREATMENT OF ALLERGIC RHINITIS

As-needed intranasal corticosteroid spray reduced allergic inflammation. It was more effective than

as-needed H1 blockers in the treatment of seasonal allergic rhinitis.

Practical point: Most patients with troublesome seasonal allergic rhinitis probably take continuing anti-histamine or intranasal steroid during the season. Choice would be personal according to trial and error comparison between the two.

12-6 EFFECT OF OMALIZUMAB ON SYMPTOMS OF SEASONAL ALLERGIC RHINITIS

Omalizumab. an IgE blocking antibody, provided significant relief from allergic rhinitis. And reduced serum free IgE levels.

Practical point: An entirely new development . Watch for additional reports.

ALZHEIMER'S DISEASE

6-4 MIDLIFE VASCULAR RISK FACTORS AND ALZHEIMER'S DISEASE IN LATER LIFE

Raised systolic BP and high cholesterol concentrations (and particularly the combination) in midlife were associated with increased risk of Alzheimer's disease later in life. This possible added benefit would be most welcome.

Practical point: Both factors should be controlled in mid-life regardless of any possible benefit on reducing risk of Alzheimer's. Control of both to reduce risk of cardiovascular disease is one of the great challenges and opportunities for primary care clinicians. Any possible reduction in incidence of Alzheimer's would be an additional benefit. .

7-10 A PROSPECTIVE STUDY OF PHYSICAL ACTIVITY AND COGNITIVE DECLINE IN ELDERLY WOMEN.

Elderly women with higher levels of baseline physical activity were less likely to develop cognitive decline over the next 6 to 8 years.

Practical point: Another point for clinicians to encourage fitness over a lifetime.

11-17 NONSTEROIDAL ANTIINFLAMMATORY DRUGS AND THE RISK OF ALZHEIMER'S DISEASE

Long-term use of NSAIDs may have a beneficial effect in preventing AD. "Primary-prevention trials should be undertaken to confirm this finding and show whether the benefits of such therapy outweigh the risks."

Practical point; None at this time. We need more information on the benefit/harm-cost. Primary care clinicians should be aware of this putative linkage. Patients may be asking about it.

12-11 UNTANGLING VASCULAR DEMENTIA

Questions remain about the mechanism of the interaction between cerebrovascular disease and Alzheimer's in an individual patient. Alzheimer's disease cannot be ruled out by clinical investigation. A diagnosis of vascular dementia does not rule out Alzheimer's. The part that cerebrovascular disease may play in producing symptoms of dementia is particularly difficult to understand when it is accompanied by histological features of Alzheimer's disease.

"It is not surprising that accurate clinical diagnosis of Alzheimer's disease seems to be easier than vascular and mixed dementia. Meanwhile, it is worth noting that although 'pure' vascular dementia exists, vascular disease may be an important and potentially treatable contributor to Alzheimer's disease."

Practical point: We await untangling the pathogenesis of Alzheimer's, and have great hope for development of specific preventive measures for the disease. In the meantime, we can do a great deal to protect the vascular system of the brain. The same prophylactic measures apply to the brain as to the coronary circulation.

ANEMIA

4-12 THE ANAEMIA OF CHRONIC DISEASE.

Practical point: Is the microcytic anemia of a sick patient due to iron deficiency or to the anemia of chronic disease? Testing the soluble transferrin receptor (STR) in serum may differentiate. STR is raised in iron deficiency; normal in ACD.

6-11 WHY SHOULD WOMEN HAVE LOWER REFERENCE LIMITS FOR HAEMOGLOBIN AND FERRITIN CONCENTRATIONS THAN MEN?

"The data from humans point to the possibility that the current lower reference levels for red blood cell counts and hemoglobin and serum ferritin concentrations in women have been derived from sampling populations that are deficient in iron."

Reclassification of these parameters in women to the same values as for men would be expected to have fundamental and positive implications for women's health and welfare.

Practical point: Primary care clinicians should be aware of the near universal likelihood of iron deficiency in young women. Supplementation is reasonable.

ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACE); ANGIOTENSIN II BLOCKERS

1-18 PROPHYLACTIC TREATMENT OF MIGRAINE WITH ANGIOTENSIN CONVERTING ENZYME INHIBITOR (LISINOPRIL)

The ACE-inhibitor lisinopril had a clinically important prophylactic effect in migraine.

6-5 EFFECT OF RAMIPRIL VS AMLODIPINE IN RENAL OUTCOMES IN HYPERTENSIVE NEPHROSCLEROSIS

Practical point: African Americans with hypertension are at high risk of renal dysfunction. Obviously, do not wait for renal dysfunction to be established before beginning effective anti-hypertension therapy. We should protect the kidney as well as the heart and brain. Identifying and treating patients at the stage of microalbuminuria (20 to 200 mg/d) would lead to greater benefit than waiting for renal dysfunction to become established. Angiotensin converting enzyme inhibitors are the drugs of choice.

7-4 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND PROGRESSION OF NON-DIABETIC RENAL DISEASE: Meta-analysis of Patient-Level Data

Antihypertension regimens which include ACE inhibitors are more beneficial in slowing the progression of non-diabetic renal disease than regimens that do not contain ACE.

Practical point: Chronic renal insufficiency is under-diagnosed and under-treated. Opportunities for prevention are lost. The presence of proteinuria in chronic renal disease is a strong indication for treatment with ACE. ACE inhibitors should be the antihypertensive agents of first choice in nondiabetic renal disease as well as in diabetic renal disease.

9-8 RANDOMIZED TRIAL OF A PERINDOPRIL-BASED BLOOD-PRESSURE-LOWERING REGIMEN AMONG 6105 INDIVIDUALS WITH PREVIOUS STROKE OR TRANSIENT ISCHAEMIC ATTACK.

In patients with previous stroke or TIA, a combination of an ACE inhibitor and a diuretic lowered mean BP from about 148/86 to about 125/75 and resulted in a large reduction in risk of recurrence of stroke.

"Treatment . . . should be considered routinely for patients with a history of stroke or TIA, irrespective of their BP."

Importantly, benefit for BP lowering was evident in patients not usually considered to be hypertensive — ie, those with "high normal" BP in whom BP was lowered from a mean of 136/79 to 127/75.

Practical point: A reduction to about 125/75 would benefit without causing harm.

9-9 THE EFFECT OF IRBESARTAN ON THE DEVELOPMENT OF DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES.

In patients with type 2 diabetes, microalbuminuria, and hypertension, the angiotensin II blocker, irbesartan, was renoprotective, independent of its blood pressure lowering effect

Choice of an ACE inhibitor vs an angiotensin II blocker would depend on adverse effects (eg, cough) and cost.

Practical point: All patients with diabetes should be tested for microalbuminuria. Treatment with an ACE inhibitor or an angiotensin blocking drug should be started early.

10-5 RAMIPRIL AND THE DEVELOPMENT OF DIABETES

Ramipril, an ACE inhibitor, reduced risk of developing diabetes in high risk individuals.

12-16 BLOOD PRESSURE REDUCTION AND CARDIOVASCULAR RISK IN HOPE STUDY

The investigators concluded that ramipril confers substantial benefits *in addition* to those of other BP-lowering drugs. Benefit was greater than expected from the modest lowering of BP which occurred during the trial. But, is there really any benefit in reducing cardiovascular morbidity conferred by a drug in addition to its BP-lowering effect? Controversy remains.

Practical point: The first goal in treatment of hypertension by primary care clinicians should be lowering the BP to recommended levels -- combined by treatment of all risk factors in addition to the BP. I believe that when this is accomplished, any particular drug used will have little additional benefit. RTJ

ANOREXIA NERVOSA

6-12 DIAGNOSIS AND CARE OF PATIENTS WITH ANOREXIA NERVOSA IN PRIMARY CARE SETTINGS

Clinical diagnosis of AN is often obscure. Patients with mild cases usually seek help for non-specific symptoms such as asthenia, dizziness, and lack of energy. Presentation may be remarkable for its lack of complaints. Family members may bring patients to the physician because of concerns about amenorrhea or weight loss.

The primary care physician is often the first to consult and suspect AN. Early clinical suspicion and diagnosis is likely to lead to more effective treatment.

The primary care clinician is involved with arranging and coordinating a comprehensive and multidisciplinary treatment program.

Practical point: Suspect anorexia nervosa and bulimia in a thin young woman who exercises excessively and has amenorrhea.

ANTIBIOTICS

1-22 AN IMPORTANT NEW SERVICE FROM JOHNS HOPKINS

Hopkins has launched an antibiotic database available to all free of charge. It offers diagnostic criteria and drug options on more than 160 drugs, and 140 diseases. It is continually updated and will immediately issue emergency alerts and drug recalls. www.hopkins-abxguide.org

4-14 ANTIBIOTICS FOR ACUTE BRONCHITIS

No doubt — acute viral bronchitis does *not* respond to antibiotics. This has led to the oft repeated admonition not to prescribe antibiotics for acute bronchitis.

The editorialist point out that in a group of patients presenting with acute bronchitis, there will be a subset who have a bacterial infection, including pneumonia. The problem is how to separate those who would benefit from antibiotics from those who will not.

Practical point: Primary care clinicians must use clinical judgement to suspect those patients with acute bronchitis who have a bacterial infection. Patients who are aged, have physical signs of congestion, and who appear acutely ill are more likely to fit this category.

4-19 ANTIBIOTIC DATABASE LAUNCHED

Johns Hopkins has a free to all peer reviewed database presenting the latest information on antibiotics and infectious diseases. (www.hopkins-abxguide.org).

Practical point: This easily accessed website should be most helpful to primary care clinicians.

ANTICOAGULATION (See also **VENOUS THROMBOSIS-THROMBOEMBOLISM)**

11-16 CHOOSING A PARENTERAL ANTICOAGULANT AGENT

Fondaparinux is derived from the activated factor X (Xa) binding moiety of unfractionated heparin.

Two studies [1,2] report that once-daily treatment initiated early in the postoperative period was more effective than LMWH in preventing venous thromboembolism after hip and knee surgery.

Fondaparinux has been approved by the FDA for prevention of thromboembolism after orthopedic surgery. (*Arixtra*)

ANTIDEPRESSANTS

5-15 MANAGEMENT OF CHRONIC TENSION-TYPE HEADACHE WITH TRICYCLIC ANTIDEPRESSANT MEDICATION, STRESS MANAGEMENT THERAPY, AND THEIR COMBINATION

Practical point: Antidepressant medication and stress management therapy were each modestly effective in treating chronic tension-type headache. Combined therapy may be more beneficial.

12-15 SIMILAR EFFECTIVENESS OF PAROXETINE, FLUOXETINE, AND SERTRALINE IN PRIMARY CARE.

Three SSRIs, Paroxetine (*Paxil*); Fluoxetine (*Prozac*); and Sertraline (*Zoloft*), were similar in effectiveness and adverse effects for depressive symptoms and domains of health-related quality of life over 9 months.

Practical point: Individual trial and error may come up with the most effective and best tolerated.

ASPIRIN

1-11 LOW-DOSE ASPIRIN AND VITAMIN E IN PEOPLE AT CARDIOVASCULAR RISK: A Randomised Trial in General Practice.

In women and men at risk of having a cardiovascular event because of the presence of at least one major risk factor, low-dose aspirin was effective when given as primary prevention.

Lack of effectiveness of vitamin E is consistent with other trials on secondary prevention.

8-6 EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

The anti-platelet agent clopidogrel (*Plavix*) given in addition to aspirin, had significant benefits in patients with acute coronary syndromes without ST elevation. The risk of major bleeding was increased.

Practical point: Primary care clinicians and their patients should consider the benefit/harm/cost ratio of clopidogrel. Harms are significant, costs high. but benefits may be life saving. The stakes are high.

9-5 ASPIRIN USE AND ALL-CAUSE MORTALITY AMONG PATIENTS BEING EVALUATED FOR KNOWN OR SUSPECTED CORONARY ARTERY DISEASE. A Propensity Analysis

Aspirin use among patients suspected of CAD was independently associated with reduced long-term all-cause mortality, particularly among older patients, those with known CAD, and those with impaired exercise capacity.

Practical point: Prophylactic low-dose aspirin will benefit individuals at higher risk of CVD. For those at low risk, harms outweigh benefits. The challenge for primary care clinicians is to judge the risk.

12-10 CYCLO-OXYGENASE INHIBITORS AND THE ANTIPLATELET EFFECTS OF ASPIRIN

Ibuprofen (*Motrin; Advil*) competitively inhibited the prophylactic (anti-thrombotic) effects of aspirin.

Acetaminophen, COX-2 inhibitors, and diclofenac did not have this antagonistic effect.

Practical point: Patients taking low-dose aspirin for primary or secondary prevention of CVD should avoid ibuprofen.

ASTHMA

6-22 THUNDERSTORMS AND ASTHMA

During a thunderstorm, a downdraft of air sweeps up pollen and other particles and concentrates them in a shallow band of air at ground level. Patients with asthma should note any association with weather patterns, and take air-conditioned shelter if possible.

Practical point: In individual patients, primary care clinicians might determine the incidence of exacerbations of asthma related to weather. Recommendations to avoid outdoor air during storm times might be appropriate.

11-7 THE SAFETY OF INACTIVATED INFLUENZA VACCINE IN ADULTS AND CHILDREN WITH ASTHMA.

"Influenza vaccine does not worsen asthma." Current guidelines for the immunization of patients with asthma are safe. In a large diverse group of adults and children with asthma, adverse effects were no more common in those receiving flu vaccine than in those receiving placebo injections.

Practical point: Health care providers should urge patients with asthma to be immunized and thus reduce the morbidity associated with influenza. Patients may be reassured by referring them to this study.

BETA-BLOCKERS

5-6 EFFECT OF CARVEDILOL ON OUTCOME AFTER MYOCARDIAL INFARCTION IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION: THE CAPRICORN RANDOMISED TRIAL.

In patients treated long-term after an acute MI complicated by left ventricular systolic dysfunction. carvedilol,a beta-blocker, started within days after the MI, was associated with reduction in all-cause and cardiovascular mortality, and recurrent non-fatal MI. Benefits were in addition to aspirin and ACE inhibitors.

Practical point: Primary care clinicians will be following more patients taking beta-blockers. Starting low and going slow is a critical clinical application.

5-7 EXPANDING INDICATIONS FOR BETA-BLOCKERS IN HEART FAILURE

It is now clear that the interaction between the adrenergic nervous system and the failing heart is more complex than first realized. Chronic overexposure of the heart to norepinephrine causes hypertrophy, ischemia, and myocyte damage. The theory that the adrenergic system has a maladaptive role in chronic HF is supported by the salutary effects of beta-blockade on clinical outcomes demonstrated by large clinical trials.

Practical point: Beta-blockers represent an advance in the treatment of HF. They appear to be effective in patients with a wide spectrum of systolic HF — mild to severe.

These drugs must be administered cautiously and the dose escalated slowly in all patients with HF.

BRONCHITIS

4-14 ANTIBIOTICS FOR ACUTE BRONCHITIS

No doubt — acute viral bronchitis does *not* respond to antibiotics. This has led to the oft repeated admonition not to prescribe antibiotics for acute bronchitis.

The editorialist point out that in a group of patients presenting with acute bronchitis, there will be a subset who have a bacterial infection, including pneumonia. The problem is how to separate those who would benefit from antibiotics from those who will not.

Practical point: Primary care clinicians must use clinical judgement to suspect those patients with acute bronchitis who have a bacterial infection. Patients who are aged, have physical signs of congestion, and who appear acutely ill are more likely to fit this category.

CARDIOVASCULAR DISEASE

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In women and men at risk of having a cardiovascular event because of the presence of at least one major risk factor, low-dose aspirin was effective when given as primary prevention.

Lack of effectiveness of vitamin E is consistent with other trials on secondary prevention.

7-3 ALBUMINURIA AND RISK OF CARDIOVASCULAR EVENTS, DEATH, AND HEART FAILURE IN DIABETIC AND NON-DIABETIC INDIVIDUALS.

Any degree of albuminuria is a robust, independent risk factor for future cardiovascular events in individuals without DM who have increased risk factors for CVD, as well as those with DM. The risk increases as the albumin/creatinine ratio increases, starting well below the cutoff for microalbuminuria.

Practical point: Primary care clinicians should screen for albuminuria (both dipstick positive and below) in diabetic patients and high risk patients without diabetes. It is an inexpensive and rewarding prognostic indicator which calls for early intervention.

7-6 THE EFFECT OF HORMONE REPLACEMENT THERAPY ON CARDIOVASCULAR RISK FACTORS IN TYPE 2 DIABETES.

There is compelling evidence that HRT exerts beneficial effects on a number of cardiovascular risk factors in non-diabetic women. This study demonstrated its beneficial effect on women with type 2 diabetes.

Practical point: This may reassure those of us who believe HRT ultimately improves risk of CHD.

All patients with diabetes must be especially vigilant in reducing risk factors for cardiovascular disease. This includes routine use of low-dose aspirin. Use of aspirin during the first few months of HRT use, when there is increased risk of cardiovascular events, may be a reasonable strategy for non-diabetic patients as well as diabetic patients.

7-7 POSTMENOPAUSAL HORMONE USE AND SECONDARY PREVENTION OF CORONARY EVENTS IN THE NURSES' HEALTH STUDY

The risk of recurrent major coronary events seems to be increased among short-term hormone users with previous coronary disease. With continued use beyond 1 year, risk decreases to a level below the risk in non-users.

Practical point:

I believe primary care clinicians can reasonably give the following advice:

1. HRT should be started early in the premenopausal or immediate postmenopausal time period when women, because of their younger age, will have less risk of coronary events.
2. HRT might be avoided if possible even at an early age in women at high risk (eg, smokers, those with lipid disorders, hypertension).
3. Women with troublesome menopausal symptoms might be started on low dose estrogen (eg, 0.3 mg *Premarin*) until the danger period of 1 year is passed. Low-dose aspirin prophylaxis should be given.

7-8 RISK OF RECURRENT CORONARY EVENTS IN RELATION TO USE AND RECENT INITIATION OF POSTMENOPAUSAL HORMONE THERAPY

After a first myocardial infarction, use of HRT suggested a transient rise in risk of recurrent coronary events in the first 60 days. Thereafter, use of HRT (compared with non-use) suggested a reduction in risk (ie, a benefit).

Practical point: I do not believe HERS and other studies should deter primary care clinicians from prescribing HRT for most patients who opt to take them. These results reinforce the preceding study. Starting HRT at or before the menopause when women are younger, and avoiding use by those with many CVD risk factors would be prudent.

With due care, and concomitant use of aspirin for its anti-platelet effect, any increased risk in the first months would be avoided and thereafter a reduction of cardiovascular events would be likely as women grow older.

8-7 RISK OF CARDIOVASCULAR EVENTS ASSOCIATED WITH SELECTIVE COX-2 INHIBITORS.

The new selective COX2 inhibitors (rofecoxib *Vioxx*; celecoxib *Celebrex*) are pro-thrombotic. Meta-analyses thus far indicate an association with increased incidence of cardiovascular events compared with non-selective NSAIDs and placebo.

10-1 CARDIOVASCULAR PROTECTION AND BLOOD PRESSURE REDUCTION: A Meta-Analysis

On average, all antihypertensive drugs have similar long-term efficacy and safety in providing cardiovascular protection.

Compared with diuretics and beta-blockers, calcium channel blockers might protect more against stroke and less against myocardial infarction. This results in an overall cardiovascular benefit similar to that of old classes of antihypertension drugs.

11-4 IMPACT OF HIGH-NORMAL BLOOD PRESSURE ON THE RISK OF CARDIO-VASCULAR DISEASE.

High normal BP (130-139/85-89) was associated with an increased risk of cardiovascular disease.

Practical point: Would not lowering "high normal" BP (130-139/85-89) in individuals at high risk due to a combination of factors seem reasonable? Certainly, life style measures are indicated. Drug therapy should be reserved for those with multiple risk factors, addressing all factors at the same time.

12-16 BLOOD PRESSURE REDUCTION AND CARDIOVASCULAR RISK IN HOPE STUDY

The investigatorS concluded that ramipril confers substantial benefits *in addition* to those of other BP-lowering drugs. Benefit was greater than expected from the modest lowering of BP which occurred during the trial. But, is there really any benefit in reducing cardiovascular morbidity conferred by a drug in addition to its BP-lowering effect? Controversy remains.

Practical point: The first goal in treatment of hypertension by primary care clinicians should be lowering the BP to recommended levels -- combined by treatment of all risk factors in addition to the BP. I believe that when this is accomplished, any particular drug used will have little additional benefit. ACE inhibitors and angiotensin II blockers do have a special place in patients with renal disease and post myocardial infarction.

CAROTID ATHEROSCLEROSIS

1-16 CARDIORESPIRATORY FITNESS AND THE PROGRESSION OF CAROTID ATHEROSCLEROSIS IN MIDDLE-AGED MEN.

Good cardiorespiratory fitness was associated with slower progression of early carotid atherosclerosis in middle-aged men.

CAROTID STENOSIS

4-10 RISK, CAUSES, AND PREVENTION OF ISCHAEMIC STROKE IN ELDERLY PATIENTS WITH SYMPTOMATIC INTERNAL-CAROTID STENOSIS.

"If elderly people are denied therapy for reasons of prejudice and not of science, they may justifiably feel that they have been abandoned on the basis of age alone."

In the secondary prevention (after TIA or non-disabling stroke) of ipsilateral stroke, patients over age 75 with 50-99% symptomatic stenosis, benefited more from endarterectomy than younger patients.

And much more than those in the group receiving medical treatment alone.

Practical point: Elderly patients who have experienced a TIA or non-disabling stroke are at extremely high risk of a second stroke. Since the elderly live now live longer than in the past, in patients over age 75 the benefits of surgery may outweigh the risks of surgery and of continued medical treatment. They should be informed about the local experience of endarterectomy and given the opportunity to choose for themselves.

10-2 EXTRACRANIAL CAROTID STENOSIS

Symptomatic CS

All should receive antiplatelet medication: aspirin, clopidogrel (*Plavex*), or the combination of aspirin and dipyridamole. Anticoagulant therapy is not routinely recommended.

Endarterectomy: Indicated for patients with 70% to 99% stenosis who are good candidates for surgery and have had symptoms within the past 2 years. For those with 50% to 69% stenosis decision for surgery should be made on the clinical features that influence risk of stroke vs the risks of surgery.

Asymptomatic CS:

Surgery should be individualized and considered for those under age 80 with stenosis > 60% if an experienced surgeon is available. Presence or absence of coexisting conditions, life expectancy, and patient preferences should be considered.

10-3 TRANSIENT MONOCULAR BLINDNESS ASSOCIATED WITH CAROTID ARTERY STENOSIS.

As compared with hemispheric TIA, TMB associated with internal carotid stenosis carries a better prognosis with respect to subsequent stroke. Endarterectomy may improve prognosis in the group with other risk factors for stroke.

Practical point: This does have some clinical application to primary care. Patients with TMB may be informed more accurately about prognosis. Clinician and patient may more easily reach agreement about treatment.

CERVICAL CANCER

1-13 CHLAMYDIA AND CERVICAL CANCER

C trachomatis is already known to be associated with pelvic inflammatory disease, infertility, and facilitation of transmission of HIV infection. Cervical cancer may be another complication.

5-10 CURRENT APPROACHES TO CERVICAL-CANCER SCREENING

Although screening saves lives, there is no consensus about when screening should start, how long it should continue, the frequency of screening, or the optimal screening technique. Information needed to make informed decisions is, in many respects, incomplete. The article offers suggestions and guidelines.

12-2 PERSISTENT HUMAN PAPILLOMAVIRUS INFECTION AS A PREDICTOR OF CERVICAL INTRAEPITHELIAL NEOPLASIA

The study adds to the body of evidence strongly implicating persistent HPV infections, particularly with oncogenic strains, as a cause of SIL.

"A strong relationship exists between *persistent* HPV infection and SIL incidence, especially for HPV types 16 and 18."

The study adds to the body of evidence strongly implicating persistent HPV infections, particularly with oncogenic strains, as a cause of SIL.

The investigators support the application of repeated type-specific HPV DNA testing in screening for SIL (and by implication prevention of cervical cancer). Vaccines against oncogenic strains (especially type 16 and 18) are a potential for prevention.

Practical point: Watch for developments. Is this the next major step in cancer prevention?

CHLAMYDIA

1-13 CHLAMYDIA AND CERVICAL CANCER

C trachomatis is already known to be associated with pelvic inflammatory disease, infertility, and facilitation of transmission of HIV infection. Cervical cancer may be another complication.

CHRONIC OBSTRUCTIVE LUNG DISEASE

5- 18 ORAL MUCOLYTIC DRUGS

Practical Point: A trial of oral mucolytics may be worthwhile in patients with severe COPD.

CLINICAL INERTIA

11-2 CLINICAL INERTIA

Medicine has traditionally focused on relieving patient symptoms. However, maintaining good health increasingly involves management of such problems as hypertension, dyslipidemia, and diabetes, which often have no symptoms. Abnormal BP, lipid, and glucose values are generally sufficient to warrant treatment without further diagnostic maneuvers. These commentators focus on limitations in managing such problems in everyday practice. They term this "clinical inertia"-- recognition of the problem but failure to act -- failure of clinicians to initiate or intensify therapy when indicated.

CLOPIDOGREL (*Plavix*)

4-4 RESULTS OF CURE TRIAL FOR ACUTE CORONARY SYNDROME

Clopidogrel (*Plavix*— an antiplatelet drug), acts to inhibit adenosine diphosphate, an activator of platelet aggregation.

This randomized, double-blind trial entered over 12 500 patients with acute coronary syndromes. For every 1000 persons treated for 9 months, an estimated 28 cardiovascular deaths, MIs, or strokes would be prevented.

Practical point: The treatment of acute coronary events, including myocardial infarction, is in a state of flux. Use of thrombolysis is giving way to use of platelet inhibitors and early coronary revascularization. Primary care clinicians should be able to identify patients with acute coronary syndromes and begin treatment as early as possible. They should correlate the best current treatment with their cardiologist consultants. Watch for evolving developments.

8-6 EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

The anti-platelet agent clopidogrel (*Plavix*) given in addition to aspirin, had significant benefits in patients with acute coronary syndromes without ST elevation. The risk of major bleeding was increased.

Practical point: Primary care clinicians and their patients should consider the benefit/harm/cost ratio of clopidogrel. Harms are significant, costs high. but benefits may be life saving. The stakes are high.

COLORECTAL CANCER

8-9 ONE-TIME SCREENING FOR COLORECTAL CANCER WITH COMBINED FECAL OCCULT-BLOOD TESTING AND EXAMINATION OF THE DISTAL COLON

One-time screening of asymptomatic subjects with FBOT plus sigmoidoscopy failed to identify about 1 of every 4 subjects with advanced neoplasia.

Practical point: Primary care clinicians should advise all patients over 50 to undergo periodic colonoscopy and omit FBOT and sigmoidoscopy.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

7-14 CAM RESEARCH ATTEMPTS TO SEPARATE WHEAT FROM CHAFF

The National Center for Complementary and Alternative Medicine (part of the NIH) is attempting to develop a more thorough understanding of how herbs react in the body.

Several multicenter, randomized trials are being conducted. Primary care clinicians should watch for developments.

7-15 HERBAL MEDICINES AND PERIOPERATIVE CARE.

Many potential adverse effects may occur in patients taking herbal medicines before surgery.

During the perioperative evaluation, physicians should explicitly elicit and document a history of herbal medicine use.

Practical point: Primary care clinicians should be familiar with potential adverse effects of complementary-alternative medicines in order to recognize, prevent, and treat serious problems associated with their use.

CORONARY HEART DISEASE

1-1 GLYCATED HAEMOGLOBIN, DIABETES, AND MORTALITY IN MEN IN NORFOLK COHORT OF EUROPEAN PROSPECTIVE INVESTIGATION OF CANCER AND NUTRITION (EPIC-Norfolk)

Over 2 to 4 years, glycosylated hemoglobin concentration was a graded, continuous risk factor for death. Every increase of 1% in HbA1c above 5% was associated with a 29% increase in risk of all-cause death; a 38% increase in cardiovascular mortality; and 44% increase in ischemic heart disease mortality.

Adequate screening for impairments in glucose metabolism should include a HbA1c in addition to a fasting plasma glucose, at least if the glucose is over 110.

1-2 "NORMAL" BLOOD GLUCOSE AND CORONARY RISK:

Glycosylated hemoglobin provides a reliable estimate of usual glycemia and should be a more precise predictor of CHD risk. Glucose control for CHD prevention should begin in those with impaired glucose tolerance (110 to 125 mg/dL).

4-7 EFFECTS OF ATORVASTATIN ON EARLY RECURRENT ISCHEMIC EVENTS IN ACUTE CORONARY SYNDROMES: The MIRACL Study

High dose atorvastatin started within 1 to 3 days after presentation for acute coronary syndromes was associated with a reduction in risk of early recurrent ischemic events, but with no other significant clinical benefit.

Practical point: Statin drugs given immediately after onset of acute myocardial infarction or unstable angina may be associated with only small benefits over 4 months. Nevertheless, statins should be started for secondary prevention and maintained over years. Starting early in the hospital will encourage compliance.

4-8 EFFECT OF LIPID-LOWERING THERAPY ON EARLY MORTALITY AFTER ACUTE CORONARY SYNDROMES.

Prescription of a lipid-controlling drug at hospital discharge for patients with unstable angina or MI, was independently associated with reduced short-term mortality over 1 month and 6 months.

Practical point: There is good reason for prescribing statin drugs to patients with acute coronary syndromes (ie, established coronary disease) during their hospitalization or at discharge.

4-9 COMPARISON OF CORONARY-ARTERY BYPASS SURGERY AND STENTING FOR THE TREATMENT OF MULTIVESSEL DISEASE

At one year, in patients with multivessel coronary disease, angioplasty with stenting and CABG offered the same protection against death, stroke, and MI. Stenting was less costly, but resulted in more revascularization procedures. The recent application of newer antiplatelet drugs (glycoprotein IIb/IIIa receptor blockers) may further tilt advantage toward stents.

Practical point: In areas where logistic problems have been overcome, patients may be given full information about local experience and be given a choice between CABG and stenting. Many may choose stenting because of its more timely administration and less disability-time. And because of the reported cognitive declines reported in patients undergoing CABG.

5-8 BENEFITS OF PRAVASTATIN ON CARDIOVASCULAR EVENTS AND MORTALITY IN OLDER PATIENTS WITH CORONARY HEART DISEASE ARE EQUAL TO OR EXCEED THOSE SEEN IN YOUNGER PATIENTS: The LIPID Trial

Practical point: Older persons with established coronary disease and average or moderately elevated cholesterol levels may benefit from secondary prevention with pravastatin therapy. Co-morbidity, expected length of life, and personal preference are contraindications, not age.

6-2 OPTIMAL TREATMENT OF ACUTE CORONARY SYNDROMES — An Evolving Strategy

This article summarizes the latest recommendations. A reference algorithm is presented on p 1941.

Practical point: Primary care clinicians can serve their patients optimally by immediately beginning non-interventional measures (aspirin, heparin, oral beta-blocker, and medication for pain control). Primary care clinicians remote from emergency centers must keep up with the rapid changes in therapy in order to correlate urgent treatment with their cardiologist colleagues. Each minute of myocardial ischemia adds to risk. The new bolus agents will facilitate early fibrinolysis out of hospital.

6-3 THE EFFECT OF FRUIT AND VEGETABLE INTAKE ON RISK FOR CORONARY DISEASE

The data support a protective effect of greater consumption of fruits and vegetables, particularly green leafy vegetables and vitamin C rich fruits and vegetables, against CHD.

Practical point: Primary care clinicians should repeatedly advise patients about the benefits of a healthy diet.

7-7 POSTMENOPAUSAL HORMONE USE AND SECONDARY PREVENTION OF CORONARY EVENTS IN THE NURSES' HEALTH STUDY

The risk of recurrent major coronary events seems to be increased among short-term hormone users with previous coronary disease. With continued use beyond 1 year, risk decreases to a level below the risk in non-users.

Practical point:

I believe primary care clinicians can reasonably give the following advice:

1. HRT should be started early in the premenopausal or immediate postmenopausal time period when women, because of their younger age, will have less risk of coronary events.
2. HRT might be avoided if possible even at an early age in women at high risk (eg, smokers, those with lipid disorders, hypertension).
3. Women with troublesome menopausal symptoms might be started on low dose estrogen (eg, 0.3 mg *Premarin*) until the danger period of 1 year is passed. Low-dose aspirin prophylaxis should be given.

7-8 RISK OF RECURRENT CORONARY EVENTS IN RELATION TO USE AND RECENT INITIATION OF POSTMENOPAUSAL HORMONE THERAPY

After a first myocardial infarction, use of HRT suggested a transient rise in risk of recurrent coronary events in the first 60 days. Thereafter, use of HRT (compared with non-use) suggested a reduction in risk (ie, a benefit).

Practical point: I do not believe HERS and other studies should deter primary care clinicians from prescribing HRT for most patients who opt to take them. These results reinforce the preceding study. Starting HRT at or before the menopause when women are younger, and avoiding use by those with many CVD risk factors would be prudent.

With due care, and concomitant use of aspirin for its anti-platelet effect, any increased risk in the first months would be avoided and thereafter a reduction of cardiovascular events would be likely as women grow older.

7-11 ACUTE EFFECTS OF PASSIVE SMOKING ON THE CORONARY CIRCULATION IN HEALTHY YOUNG ADULTS.

Passive smoking substantially reduced coronary blood flow reserve in healthy non-smokers. Passive smoking may cause endothelial dysfunction in the coronary circulation in non-smokers.

This should convince the diehards who still maintain that harms of passive smoking are not proven. It strengthens the resolve of those who oppose smoking in public places

9-5 ASPIRIN USE AND ALL-CAUSE MORTALITY AMONG PATIENTS BEING EVALUATED FOR KNOWN OR SUSPECTED CORONARY ARTERY DISEASE. A Propensity Analysis

Aspirin use among patients suspected of CAD was independently associated with reduced long-term all-cause mortality, particularly among older patients, those with known CAD, and those with impaired exercise capacity.

Practical point: Prophylactic low-dose aspirin will benefit individuals at higher risk of CVD. For those at low risk, harms outweigh benefits. The challenge for primary care clinicians is to judge the risk.

9-16 ROLE OF INFLAMMATORY BIOMARKERS IN PREDICTION OF CORONARY HEART DISEASE.

C-reactive protein, is a strong and independent predictor of future vascular events. Measurement of this inflammatory marker adds to the predictive value of standard lipid screening, particularly in primary prevention. The greater prognostic utility of C-reactive protein reflects the long half-life and stability of the molecule. This is coupled with a lack of circadian variation and low coefficients of variation when measured by high sensitivity assays.

Practical point: CRP has not yet been included in the usual risk markers. CRP is of potential future interest. We await clarification. Primary care clinicians — keep it in mind.

11-6 SIMVASTATIN AND NIACIN, ANTIOXIDANT VITAMINS, OR THE COMBINATION FOR THE PREVENTION OF CORONARY DISEASE.

Compared with placebo, combined niacin-statin (simvastatin) provided marked clinical and angiographic benefits in patients with established coronary disease and low HDL levels. (Secondary prevention). The decrease in LDL related to combined statin-niacin was greater than the average decrease reported from statin therapy alone. The increase in HDL was much more than usually reported from statins alone. The rate of major clinical events was reduced by 90% in the simvastatin + niacin group.

Antioxidants did not benefit. "Unless more compelling evidence appears, we see little justification for the use of antioxidant vitamins for the prevention of cardiovascular events."

11-10 LEGUME CONSUMPTION AND RISK OF CORONARY HEART DISEASE IN US MEN AND WOMEN

A significant benefit in reducing incidence of cardiovascular disease was associated with increased legume consumption of at least 4 servings weekly.

11-11 DECREASED RATE OF CORONARY RESTENOSIS AFTER LOWERING OF PLASMA HOMOCYSTEINE LEVELS.

Treatment with a combination of folic acid (400ug), vitamin B12 (400 ug) and B6 (pyridoxine 10 mg) was associated with a significant reduction in the rate of restenosis after PTCA.

12-7 TOTAL CHOLESTEROL/HDL-CHOLESTEROL RATIO VS LDL-CHOLESTEROL/HDL-CHOLESTEROL RATIO AS INDICES OF ISCHEMIC HEART RISK IN MEN

In addition to the well-established conventional risk factors, the Total-c/HDL-c ratio may represent an important cumulative index of the presence of an atherogenic dyslipidemic profile associated with insulin resistance.

It was a simple index of IHD risk in men in this study.

Calculation of the LDL-c/HDL-c ratio may underestimate IHD risk in some patients since it ignores any contribution of the cholesterol in triglycerides.

Practical point: This may be a valid alternative to risk assessment. Calculation or determination of LDL-c may be eliminated, making assessment simpler.

CYCLO-OXYGENASE INHIBITORS; COX-2 INHIBITORS.

8-7 RISK OF CARDIOVASCULAR EVENTS ASSOCIATED WITH SELECTIVE COX-2 INHIBITORS.

The new selective COX2 inhibitors (rofecoxib *Vioxx*; celecoxib *Celebrex*) are pro-thrombotic. Meta-analyses thus far indicate an association with increased incidence of cardiovascular events compared with non-selective NSAIDs and placebo.

Practical point: COX-2 inhibitors should be used with caution in patients with established coronary disease and those at high risk of atherosclerosis.

12-10 CYCLO-OXYGENASE INHIBITORS AND THE ANTIPLATELET EFFECTS OF ASPIRIN

Ibuprofen (*Motrin; Advil*) competitively inhibited the prophylactic (anti-thrombotic) effects of aspirin.

Acetaminophen, COX-2 inhibitors, and diclofenac did not have this antagonistic effect.

Practical point: Patients taking low-dose aspirin for primary or secondary prevention of CVD should avoid ibuprofen.

C-REACTIVE PROTEIN

1-14 THE RENAISSANCE OF C REACTIVE PROTEIN

Routine empirical measurement of CRP is a valuable aid to patient management across a broad range of clinical practice. Sensitive assay may become a new risk assessment marker for cardiovascular disease. A raised level in patients with active coronary disease identifies a high risk group likely to require interventions. "Possibly the more C reactive protein you produce, the sicker you get."

9-16 ROLE OF INFLAMMATORY BIOMARKERS IN PREDICTION OF CORONARY HEART DISEASE.

C-reactive protein, is a strong and independent predictor of future vascular events. Measurement of this inflammatory marker adds to the predictive value of standard lipid screening, particularly in primary prevention. The greater prognostic utility of C-reactive protein reflects the long half-life and stability of the molecule. This is coupled with a lack of circadian variation and low coefficients of variation when measured by high sensitivity assays.

Practical point: CRP has not yet been included in the usual risk markers. CRP is of potential future interest. We await clarification. Primary care clinicians — keep it in mind.

DEFIBRILLATION

6-16 DO DOCTORS POSITION DEFIBRILLATION PADDLES CORRECTLY?

The International Liaison Committee of Resuscitation guidelines specify placement of the centers of the two paddles:

Sternal paddle — below the **right** clavicle in the mid-clavicular line

Apical paddle — to the left of the nipple with the center of the electrode in the mid-axillary line.

DEMENTIA (See also ALZHEIMER'S DISEASE)

7-10 A PROSPECTIVE STUDY OF PHYSICAL ACTIVITY AND COGNITIVE DECLINE IN ELDERLY WOMEN.

Elderly women with higher levels of baseline physical activity were less likely to develop cognitive decline over the next 6 to 8 years.

Practical point: Another point for clinicians to encourage fitness over a lifetime.

12-11 UNTANGLING VASCULAR DEMENTIA

Questions remain about the mechanism of the interaction between cerebrovascular disease and Alzheimer's in an individual patient. Alzheimer's disease cannot be ruled out by clinical investigation. A diagnosis of vascular dementia does not rule out Alzheimer's. The part that cerebrovascular disease may play in producing symptoms of dementia is particularly difficult to understand when it is accompanied by histological features of Alzheimer's disease.

"It is not surprising that accurate clinical diagnosis of Alzheimer's disease seems to be easier than vascular and mixed dementia. Meanwhile, it is worth noting that although 'pure' vascular dementia exists, vascular disease may be an important and potentially treatable contributor to Alzheimer's disease."

Practical point: We await untangling the pathogenesis of Alzheimer's, and have great hope for development of specific preventive measures for the disease. In the meantime, we can do a great deal to protect the vascular system of the brain. The same prophylactic measures apply to the brain as to the coronary circulation.

DEPRESSION

6-14 SMOKING CESSATION AND THE COURSE OF MAJOR DEPRESSION

Smokers with a history of depression who abstained from smoking were at high risk of developing a new episode of major depression.

Practical point: How should primary care clinicians respond to this information? Which is worse -- continuing smoking or developing another episode of major depression? Is cigarette smoking always bad? Obviously, millions of persons choose to smoke fully knowing the risks. There must be some benefit. Relentlessly pushing some patients to stop smoking could drive them away. A frank discussion about pros and cons might lead to a trial of nicotine replacement.

12-15 SIMILAR EFFECTIVENESS OF PAROXETINE, FLUOXETINE, AND SERTRALINE IN PRIMARY CARE.

Three SSRIs, Paroxetine (*Paxil*); Fluoxetine (*Prozac*); and Sertraline (*Zoloft*), were similar in effectiveness and adverse effects for depressive symptoms and domains of health-related quality of life over 9 months.

Practical point: Individual trial and error may come up with the most effective and best tolerated.

DIABETES

1-1 GLYCATED HAEMOGLOBIN, DIABETES, AND MORTALITY IN MEN IN NORFOLK COHORT OF EUROPEAN PROSPECTIVE INVESTIGATION OF CANCER AND NUTRITION (EPIC-Norfolk)

Over 2 to 4 years, glycosylated hemoglobin concentration was a graded, continuous risk factor for death. Every increase of 1% in HbA1c above 5% was associated with a 29% increase in risk of all-cause death; a 38% increase in cardiovascular mortality; and 44% increase in ischemic heart disease mortality.

Adequate screening for impairments in glucose metabolism should include a HbA1c in addition to a fasting plasma glucose, at least if the glucose is over 110.

1-2 "NORMAL" BLOOD GLUCOSE AND CORONARY RISK

Glycosylated hemoglobin provides a reliable estimate of usual glycemia and should be a more precise predictor of CHD risk. Glucose control for CHD prevention should begin in those with impaired glucose tolerance (110 to 125 mg/dL).

4-1 HOW DO YOU DEFINE DIABETES?

The American Diabetes Society and the World Health Organization define "diabetes", "impaired fasting glucose" and "impaired glucose tolerance" differently. Primary care physicians must be aware of the sometimes modest changes in glucose metabolism which can lead to later development of diabetes and its devastating consequences. The abstract presents definitive cut points for glucose levels.

Practical point: This is an important reference for primary care clinicians. We must be attuned to milder abnormalities of glucose concentration. Frequently this gives the best opportunity to improve lifestyles to lessen the risk of future development of harmful effects of elevated glucose concentrations.

4-2 RELATION OF IMPAIRED FASTING AND POSTLOAD GLUCOSE WITH INCIDENT TYPE 2 DIABETES IN A DUTCH POPULATION: The Hoorn Study

The cumulative incidence of diabetes was strongly related to both impaired fasting plasma glucose and impaired glucose tolerance, and, in particular, the combined presence of both.

Practical point: A fasting plasma glucose of 110 to 125 will predict a high risk of later progression to diabetes. An impaired glucose tolerance (post challenge glucose of 140-200 will also predict high risk. The combination of both will predict almost inevitable progression to diabetes over the years.

Early determination of these defects in glucose metabolism permits clinicians to emphasize the importance of lifestyle changes to retard development of diabetes. The cumulative incidence of diabetes was strongly related to both impaired fasting plasma glucose and impaired glucose tolerance, and, in particular, the combined presence of both.

5-2 PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

Type 2 diabetes can be prevented by changes in the lifestyle of patients with impaired glucose tolerance

Although the average amount of weight lost was not large, the difference between groups in incidence of diabetes was substantial. Even a relatively small loss of 5% of weight was important. The conservative target of more than 4 hours of exercise per week was

associated with a significant reduction in risk. "The reasonably low dropout rate in our study indicates that subjects with impaired glucose tolerance are willing and able to participate in a demanding intervention program."

Practical point: This is an important study. Glucose metabolism should be checked in older patients. Discovery of moderate abnormalities (impaired fasting glucose and impaired glucose tolerance) will provide an excellent opportunity to encourage patients to modify their lifestyles.

7-3 ALBUMINURIA AND RISK OF CARDIOVASCULAR EVENTS, DEATH, AND HEART FAILURE IN DIABETIC AND NON-DIABETIC INDIVIDUALS.

Any degree of albuminuria is a robust, independent risk factor for future cardiovascular events in individuals without DM who have increased risk factors for CVD, as well as those with DM. The risk increases as the albumin/creatinine ratio increases, starting well below the cutoff for microalbuminuria.

Practical point: Primary care clinicians should screen for albuminuria (both dipstick positive and below) in diabetic patients and high risk patients without diabetes. It is an inexpensive and rewarding prognostic indicator which calls for early intervention.

7-6 THE EFFECT OF HORMONE REPLACEMENT THERAPY ON CARDIOVASCULAR RISK FACTORS IN TYPE 2 DIABETES.

There is compelling evidence that HRT exerts beneficial effects on a number of cardiovascular risk factors in non-diabetic women. This study demonstrated its beneficial effect on women with type 2 diabetes.

Practical point: This may reassure those of us who believe HRT ultimately improves risk of CHD.

All patients with diabetes must be especially vigilant in reducing risk factors for cardiovascular disease. This includes routine use of low-dose aspirin. Use of aspirin during the first few months of HRT use, when there is increased risk of cardiovascular events, may be a reasonable strategy for non-diabetic patients as well as diabetic patients.

9-1 DIET, LIFESTYLE, AND THE RISK OF TYPE 2 DIABETES MELLITUS IN WOMEN.

Most cases of type 2 diabetes could be prevented by a healthy lifestyle: weight control, regular exercise, modification of diet, abstinence from smoking, and limited consumption of alcohol.

Weight control would appear to offer the greatest benefit.

9-2 EFFECTS OF EXERCISE ON GLYCEMIC CONTROL AND BODY MASS INDEX IN TYPE 2 DIABETES MELLITUS

Exercise programs per se, both resistance and aerobic, over a 4 month period resulted in a reduction in HbA1c of a magnitude likely to be of clinical significance. .

Practical points:

A. Exercise improved HbA1c, not dependent on weight loss.

B. Resistance exercise was also of value, especially applicable to patients who cannot walk.

C. Patients can be told as little as 4 months of consistent exercise 3 to 4 times weekly will benefit.

D. Exercise per se is likely to be beneficial in preventing development of type 2 diabetes in patients with impaired glucose tolerance or elevated fasting glucose levels not now considered as having type 2 diabetes.

9-3 INSULINS TODAY AND BEYOND

"Insulin glargine (*Lantus*) as the basal insulin combined with rapid acting analogues (*Humalog*) is probably the most physiological insulin substitution therapy and will therefore be the basis for future comparisons."

Practical point: In difficult-to-control diabetics, the combination will more likely reduce the HbA1c toward normal.

9-9 THE EFFECT OF IRBESARTAN ON THE DEVELOPMENT OF DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES.

In patients with type 2 diabetes, microalbuminuria, and hypertension, the angiotensin II blocker, irbesartan, was renoprotective, independent of its blood pressure lowering effect

Choice of an ACE inhibitor vs an angiotensin II blocker would depend on adverse effects (eg, cough) and cost.

Practical point: All patients with diabetes should be tested for microalbuminuria. Treatment with an ACE inhibitor or an angiotensin blocking drug should be started early.

10-5 RAMIPRIL AND THE DEVELOPMENT OF DIABETES

Ramipril, an ACE inhibitor, reduced risk of developing diabetes in high risk individuals.

11-1 INSULINOTROPIC MEGLITINIDE ANALOGUES: Repaglinide (*Prandin*); A New Oral Drug

New oral insulinotropic drugs are coming on the market. They act quickly to release insulin into the portal circulation and

liver when given shortly before meals. They reduce hyperglycemia by an immediate action on the liver which impairs glucose output. They are less likely to produce hypoglycemia. Dosing schedules may be more flexible.

DOCTOR-PATIENT RELATIONSHIP

4-13 THE DOCTOR'S LETTER OF CONDOLENCE

Practical point: Reviving the old custom of writing letters of condolence to families of deceased patients may help relieve the burden of bereavement and hasten closure for physicians as well as families. ". In this medical world, shaped by technological advances, we must maintain our humanity."

6-1 "TELL ME ABOUT YOURSELF": The Patient-Centered Interview.

Physicians should focus more attention on patient's concerns, feelings, and ideas. Inattention to the person of the patient, to the patient's characteristics and concerns, leads to inadequate clinical data-gathering, non-adherence, and poor outcomes. Each patient's experience of illness is unique. "To know what kind of a person has a disease is as essential as knowing what kind of disease a person has." The art (of listening) is long; time is short.

Practical point: Primary care physicians must go beyond disease-centeredness in the clinical encounter. They must become expert at listening without interruption and with undivided attention, and then lead patients to disclose more about themselves. RTJ

10-7 NARRATIVE MEDICINE

Narrative competence is the competence that human beings use to absorb, interpret, and respond to stories others tell. Everyone has a story to tell. Along with scientific ability, physicians need the ability to listen to the narratives of the patient, grasp and honor their meaning, and be moved to act on the patient's behalf.

10-8 "I WISH THINGS WERE DIFFERENT": EXPRESSING WISHES IN RESPONSE TO LOSS, FUTILITY, AND UNREALISTIC HOPES

"When the emotion is unrealistic hope, loss, futility, or grief that seems overwhelming or otherwise is very difficult to address, physicians should consider joining with the patient and family in the expression of a wish that their circumstances were different."

In these challenging situations physicians may attempt to respond empathetically by stating "I'm sorry". This well intentioned response, although frequently appropriate, may be misinterpreted and misdirected.

Practical point: Primary care clinicians will develop their own individual approaches when encountering difficult emotional situations. This suggestion is a worth-while approach.

10-9 OBSERVATIONAL STUDY OF EFFECT OF PATIENT CENTEREDNESS AND POSITIVE APPROACH ON OUTCOMES OF GENERAL PRACTICE CONSULTATIONS.

Patient-centered approach includes five components.

1) Communication and partnership with the doctor.
2) Personal relationship with the doctor.
3) Health promotion.
4) Positive approach to diagnosis and prognosis.
5) Interest in the effect of the illness on the patient's life.

If the doctor provides a positive patient-centered approach, patients will be more satisfied, more enabled, and may have less symptom burden and fewer rates of referral.

12-17 PHYSICIAN CHARTER OF PROFESSIONALISM

A campaign to shore up physicians' special place in society has resulted in a *Charter of Professionalism.* The charter reminds physicians that satisfying in full the expectations of a medical professional is still within their control. Physicians may lead a full and satisfying life of medicine.

The Physician Charter of Professionalism contains three fundamental principles:

Primacy of patient welfare

Patient autonomy

Social justice

12-12 ENGAGING PATIENTS IN MEDICAL DECISION MAKING

Three questions dominate the debate about the role of the patient in making treatment decisions:

Can patients take a leading role in making decisions?

Do they want to?

What if doctors and public health professionals don't like their choices?

Fully informed shared decision making is difficult to conduct in practice. Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal. "Most patients want to see the road map, including alternative routes, even if they don't want to take the wheel."

Fully informed shared decision making is difficult to conduct in practice.

Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal.

DRY EYE SYNDROME

11-14 HORMONE REPLACEMENT THERAPY AND DRY EYE SYNDROME

Postmenopausal women who used HRT had a higher prevalence of dry eye syndrome compared with never-users. Those using estrogen alone are more affected.

DYSPEPSIA

12-9 INDIGESTION: WHEN IS IT FUNCTIONAL?

Patients often complain of "indigestion". This may be defined differently by individual patients. To some it is heartburn and acid regurgitation; others may describe abdominal rumblings and belching; others, non-painful discomfort in the upper abdomen (fullness, bloating, early satiety).

"Dyspepsia" is best restricted to mean pain or discomfort centered in the upper abdomen.

There are many causes of dyspepsia. But, at least two thirds of patients have no structural or biochemical explanation for their symptoms.

It has been suggested that dyspepsia can be subdivided based on clusters of symptoms. But, subgroups have not proved to be of value in identifying the underlying cause. Symptoms overlap considerably.

Practical point: Perhaps asking patietns with troublesome dyspepsia to read this article may help them.

EAR PIERCING

4-17 "HIGH" EAR PIERCING AND THE RISING INCIDENE OF PERICHONDRITIS OF THE PINNA

Young persons who pierce the upper part of the ear may develop infection resulting in life-long ear deformity.

Practical point: We should warn our young patients about this complication, and advise them to seek early medical treatment if it arises.

EVIDENCE BASED MEDICINE

11-3 WHY GENERAL PRACTITIONERS DO NOT IMPLEMENT EVIDENCE

"General practitioners seem to regard clinical evidence as a square peg to fit a round hole in the patient's life." The process of implementation of evidence-based medicine is complex, fluid, and adaptive.

Decisions are influenced by the doctor's personal and professional experience as well as by their knowledge of and relationship with the patient.

FECAL OCCULT-BLOOD TESTING

8-9 ONE-TIME SCREENING FOR COLORECTAL CANCER WITH COMBINED FECAL OCCULT-BLOOD TESTING AND EXAMINATION OF THE DISTAL COLON

One-time screening of asymptomatic subjects with FBOT plus sigmoidoscopy failed to identify about 1 of every 4 subjects with advanced neoplasia.

Practical point: Primary care clinicians should advise all patients over 50 to undergo periodic colonoscopy and omit FBOT and sigmoidoscopy.

FITNESS

1-16 CARDIORESPIRATORY FITNESS AND THE PROGRESSION OF CAROTID ATHEROSCLEROSIS IN MIDDLE-AGED MEN.

Good cardiorespiratory fitness was associated with slower progression of early carotid atherosclerosis in middle-aged men.

7-10 A PROSPECTIVE STUDY OF PHYSICAL ACTIVITY AND COGNITIVE DECLINE IN ELDERLY WOMEN.

Elderly women with higher levels of baseline physical activity were less likely to develop cognitive decline over the next 6 to 8 years.

Practical point: Another point for clinicians to encourage fitness over a lifetime.

9-2 EFFECTS OF EXERCISE ON GLYCEMIC CONTROL AND BODY MASS INDEX IN TYPE 2 DIABETES MELLITUS

Exercise programs per se, both resistance and aerobic, over a 4 month period resulted in a reduction in HbA1c of a magnitude likely to be of clinical significance. .

Practical points:

A. Exercise improved HbA1c, not dependent on weight loss.

B. Resistance exercise was also of value, especially applicable to patients who cannot walk.

C. Patients can be told as little as 4 months of consistent exercise 3 to 4 times weekly will benefit.

D. Exercise per se is likely to be beneficial in preventing development of type 2 diabetes in patients with impaired glucose tolerance or elevated fasting glucose levels not now considered as having type 2 diabetes.

GASTRIC CANCER

9-7 HELICOBACTER INFECTION AND THE DEVELOPMENT OF GASTRIC CANCER

Gastric cancer developed in patients infected with *H pylori*, but not in uninfected patients.

Gastric cancer did not develop in any of the infected patients who received eradication therapy.

Patients with duodenal ulcers were not at risk.

Evidence is accumulating that eradication therapy is effective in prevention of gastric cancer. "Gastric cancer may in the future be viewed, like colon cancer, as largely a preventable disease." "We may need to view *H pylori* less as a beneficial commensal organism, and more as something akin to tobacco."

Practical point: *H pylori* infections should be eradicated.

GASTRO-ESOPHAGEAL REFLUX DISEASE

6-7 *HELICOBACTER PYLORI* AND SYMPTOMATIC RELAPSE OF GASTRO-ESOPHAGEAL REFLUX DISEASE

Eradication of the infection led to a benefit -- a longer asymptomatic period before relapse of symptoms.

Practical point: This study contradicts previous studies which suggested a harmful effect of eradication. Eradication therapy should be considered to reduce risk of stomach cancer, recurrence of peptic ulcer, and possibly for a slight reduction in severity of dyspepsia.

6-8 LONG-TERM OUTCOME OF MEDICAL AND SURGICAL THERAPIES FOR GASTROESOPHAGEAL REFLUX DISEASE

Antireflux surgery should *not* be advised with the expectation that patients will no longer take antisecretory drugs. It is clearly *not* a cancer-preventing procedure.

Practical point: Primary care clinicians should inform their patients with long term troublesome GERD about the long-term results of surgery vs medical treatment and allow them to decide.

HAND HYGIENE

8-4 HAND HYGIENE

Proper hand hygiene could reduce the incidence of transmission of infection. Washing with soap and water is not the only (or even the most effective) way of reducing transmission of organisms.

The Hand Hygiene group now recommends use of a alcohol-glycerol hand rubs between patients. They are quick to use (10 to 20 seconds) and can be used while walking or talking. This overcomes the objections to soap and water washing which takes time and requires presence of sinks.

Practical point: Clinicians — use this convenient, quick hand wash between patients

HEADACHE

5-15 MANAGEMENT OF CHRONIC TENSION-TYPE HEADACHE WITH TRICYCLIC ANTIDEPRESSANT MEDICATION, STRESS MANAGEMENT THERAPY, AND THEIR COMBINATION

Practical point: Antidepressant medication and stress management therapy were each modestly effective in treating chronic tension-type headache. Combined therapy may be more beneficial.

HEART FAILURE

1-12 TOLERATION OF HIGH DOSES OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS IN PATIENTS WITH CHRONIC HEART FAILURE.

ACE inhibitor therapy in most patients with HF can be successfully titrated to and maintained at high doses. More aggressive use is warranted. But start with a low dose (eg, 2.5 mg daily lisinopril) and gradually increase. Not all patients require the highest recommended dose.

4-6 MODERATE ALCOHOL CONSUMPTION AND RISK OF HEART FAILURE AMONG OLDER PERSONS.

Moderate alcohol consumption was associated with lower risk of heart failure among older persons. The observed benefits may not be entirely mediated by a reduction in risk of MI.

Practical point: Primary care clinicians must consider the consistently substantial benefits of alcohol reported by epidemiological studies. Advice must be individualized. Stable individuals who consume small amounts of alcohol daily should not be told to stop. Abstinent individuals may be told of the risks and benefits and a prescription for "one drink daily" may be considered.

5-6 EFFECT OF CARVEDILOL ON OUTCOME AFTER MYOCARDIAL INFARCTION IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION: THE CAPRICORN RANDOMISED TRIAL.

In patients treated long-term after an acute MI complicated by left ventricular systolic dysfunction. carvedilol,a beta-blocker, started within days after the MI, was associated with reduction in all-cause and cardiovascular mortality, and recurrent non-fatal MI. Benefits were in addition to aspirin and ACE inhibitors.

Practical point: Primary care clinicians will be following more patients taking beta-blockers. Starting low and going slow is a critical clinical application.

5-7 EXPANDING INDICATIONS FOR BETA-BLOCKERS IN HEART FAILURE

It is now clear that the interaction between the adrenergic nervous system and the failing heart is more complex than first realized. Chronic overexposure of the heart to norepinephrine causes hypertrophy, ischemia, and myocyte damage. The theory that the adrenergic system has a maladaptive role in chronic HF is supported by the salutary effects of beta-blockade on clinical outcomes demonstrated by large clinical trials.

Practical point: Beta-blockers represent an advance in the treatment of HF. They appear to be effective in patients with a wide spectrum of systolic HF — mild to severe.

These drugs must be administered cautiously and the dose escalated slowly in all patients with HF.

7-3 ALBUMINURIA AND RISK OF CARDIOVASCULAR EVENTS, DEATH, AND HEART FAILURE IN DIABETIC AND NON-DIABETIC INDIVIDUALS.

Any degree of albuminuria is a robust, independent risk factor for future cardiovascular events in individuals without DM who have increased risk factors for CVD, as well as those with DM. The risk increases as the albumin/creatinine ratio increases, starting well below the cutoff for microalbuminuria.

Practical point: Primary care clinicians should screen for albuminuria (both dipstick positive and below) in diabetic patients and high risk patients without diabetes. It is an inexpensive and rewarding prognostic indicator which calls for early intervention.

8-12 PROGNOSTIC IMPORTANCE OF ELEVATED JUGULAR VENOUS PRESSURE AND A THIRD HEART SOUND IN PATIENTS WITH HEART FAILURE.

Detection of elevated jugular venous pressure or a third heart sound in patients with HF was associated with adverse outcomes including progression of HF.

Practical point: The physical examination identifies a subset of patients with a poor prognosis who would benefit from heightened therapeutic interventions.

8-13 THE JUGULAR VENOUS PULSE AND THIRD HEART SOUND IN PATIENTS WITH HEART FAILURE

Read the description of the jugular venous pulse described by Mackenzie in 1903.

10-16 CONGESTIVE HEART FAILURE TREATMENT

The FDA has approved nesiritide (*Natrecor*), a preparation of human B-type natriuretic peptide, for intravenous treatment of acutely decompensated congestive heart failure (ADCHF).

HELICOBACTER PYLORI

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Practical point: This study contradicts previous studies which suggested a harmful effect of eradication. Eradication therapy should be considered to reduce risk of stomach cancer, recurrence of peptic ulcer, and possibly for a slight reduction in severity of dyspepsia.

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Practical point: *H pylori* infections should be eradicated.

10-17 EPIDEMIOLOGY AND DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION.

A brief explanation of the pathophysiology of *H pylori* gastritis. Why do some develop duodenal ulcers and some develop gastric ulcers and cancer?

HEMATURIA

4-11 HAEMATURIA IN ASYMPTOMATIC INDIVIDUALS

Hematuria is often detected incidentally by "dipstick". It is common. Should hematuria in asymptomatic individuals always be investigated or should it be disregarded?

In most cases the next step is to examine the urine by phase contrast microscopy to confirm the hematuria and to determine whether the red cells have originated from the glomerulus or elsewhere in the urinary tract. "Dysmorphic" or "glomerular" red cells are present when there is glomerulonephritis with proliferative features. "Non-glomerular" red cells appear when the bleeding comes from elsewhere in the urinary tract – usually infections, stones, or a tumor.

Renal biopsy most often shows "*thin basement membrane disease*". Prognosis is excellent.

Practical point: Primary care clinicians should be aware of this entity. It may save patients much anxiety and useless investigations

HEMOPHILIA

6-20 GENE THERAPY FOR HEMOPHILIA

An article in this issue of NEJM reports results of introduction of a factor VIII gene into skin fibroblasts ex vivo and then implanting the cells into the peritoneal cavity of patients with hemophilia. Detectable levels of factor VIII appeared in the serum of patients who received such cells. Therapeutic levels persisted for several months.

Practical Point: None at present. I abstracted the article because of the promise of a great leap forward in therapy of a historically devastating disease.

HEPATITIS

1-15 VIRAL HEPATITIS

A refresher course. See the abstract.

9-17 PEGINTERFERON ALFA-2B PLUS RIBAVIRIN COMPARED WITH INTERFERON ALFA-2B PLUS RIBAVIRIN FOR INITIAL TREATMENT OF CHRONIC HEPATITIS C

The most effective therapy for patients with chronic hepatitis C was peginterferon (a new compound of interferon with polyethylene glycol) once weekly combined with oral ribavirin. The benefit was mainly in patients with type 1 infection.

Practical point: The prevalence of hepatitis C is high. Primary care clinicians should be able to refer patients for the best therapy.

HOMOCYSTEINE

11-11 DECREASED RATE OF CORONARY RESTENOSIS AFTER LOWERING OF PLASMA HOMOCYSTEINE LEVELS.

Treatment with a combination of folic acid (400ug), vitamin B12 (400 ug) and B6 (pyridoxine 10 mg) was associated with a significant reduction in the rate of restenosis after PTCA.

HORMONE REPLACEMENT THERAPY

7-6 THE EFFECT OF HORMONE REPLACEMENT THERAPY ON CARDIOVASCULAR RISK FACTORS IN TYPE 2 DIABETES.

There is compelling evidence that HRT exerts beneficial effects on a number of cardiovascular risk factors in non-diabetic women. This study demonstrated its beneficial effect on women with type 2 diabetes.

Practical point: This may reassure those of us who believe HRT ultimately improves risk of CHD.

All patients with diabetes must be especially vigilant in reducing risk factors for cardiovascular disease. This includes routine use of low-dose aspirin. Use of aspirin during the first few months of HRT use, when there is increased risk of cardiovascular events, may be a reasonable strategy for non-diabetic patients as well as diabetic patients.

7-7 POSTMENOPAUSAL HORMONE USE AND SECONDARY PREVENTION OF CORONARY EVENTS IN THE NURSES' HEALTH STUDY

The risk of recurrent major coronary events seems to be increased among short-term hormone users with previous coronary disease. With continued use beyond 1 year, risk decreases to a level below the risk in non-users.

Practical point:

I believe primary care clinicians can reasonably give the following advice:

1. HRT should be started early in the premenopausal or immediate postmenopausal time period when women, because of their younger age, will have less risk of coronary events.
2. HRT might be avoided if possible even at an early age in women at high risk (eg, smokers, those with lipid disorders, hypertension).
3. Women with troublesome menopausal symptoms might be started on low dose estrogen (eg, 0.3 mg *Premarin*) until the danger period of 1 year is passed. Low-dose aspirin prophylaxis should be given.

7-8 RISK OF RECURRENT CORONARY EVENTS IN RELATION TO USE AND RECENT INITIATION OF POSTMENOPAUSAL HORMONE THERAPY

After a first myocardial infarction, use of HRT suggested a transient rise in risk of recurrent coronary events in the first 60 days. Thereafter, use of HRT (compared with non-use) suggested a reduction in risk (ie, a benefit).

The "HERS" trial (Randomized Trial of Estrogen Plus Progestin in Secondary Prevention of Coronary Heart Disease in Postmenopausal Women JAMA 1998; 280: 605-13) reported increased risk of recurrent episodes of CHD in a secondary prevention trial. . All were at high risk because of a past history of coronary heart disease.

Practical point: I do not believe HERS and other studies should deter primary care clinicians from prescribing HRT for most patients who opt to take them. These results reinforce the preceding study. Starting HRT at or before the menopause when women are younger, and avoiding use by those with many CVD risk factors would be prudent.

With due care, and concomitant use of aspirin for its anti-platelet effect, any increased risk in the first months would be avoided and thereafter a reduction of cardiovascular events would be likely as women grow older.

8-3 HORMONE REPLACEMENT THERAPY AND LONGITUDINAL CHANGES IN BLOOD PRESSURE IN POSTMENOPAUSAL WOMEN

Postmenopausal women taking HRT had a smaller increase in systolic BP over time than non-users. The difference increased with age.

Practical point: Primary care clinicians may consider this another mechanism for the protective effect of HRT. For those clinicians who believe the benefits of HRT outweigh the harms, another reason to prescribe it.

8-11 BONE MINERAL DENSITY RESPONSE TO ESTROGEN REPLACEMENT IN FRAIL ELDERLY WOMEN

In physically frail women, mean age 82, 9 months of HRT significantly increased BMD.

Traditional thought has been that the estrogen-dependent compartment of bone becomes depleted approximately 15 years after menopause. This concept has been challenged by those who believe that estrogen deficiency is also primarily responsible for the continuing decline in BMD that previously had been attributed to aging.

It was once commonly believed that bone turnover remained elevated for only a few years after menopause and that bone loss subsequently slowed or ceased in older women. Recent studies provide evidence that bone turnover remains elevated into old age

and that bone loss may accelerate rather than slow in the elderly. (Subjects in this study had high rates of bone turnover as indicated by serum and urine markers.)

Practical point; Primary care clinicians should inform their elderly female patients of the possibility that bone sparing therapy is effective regardless of age, and allow them to make an informed choice to accept or reject.

11-14 HORMONE REPLACEMENT THERAPY AND DRY EYE SYNDROME

Postmenopausal women who used HRT had a higher prevalence of dry eye syndrome compared with never-users. Those using estrogen alone are more affected.

HUMAN PAPILLOMA VIRUS

6-9 NATURAL HISTORY OF CERVICAL HUMAN PAPILLOMAVIRUS INFECTION IN YOUNG WOMEN: A Longitudinal Cohort Study

In this cohort of young women, only limited inferences could be drawn from the characteristics of HPV status at a single point in time. Longer observation in older women is needed.

Attempts to exploit the association between HPV and cervical intraepithelial neoplasia (CIN) to improve effectiveness of screening is limited. Any lead time (time from detection of HPV to development of CIN) gained by detecting HPV is likely to be short.

6-10 NATURAL HISTORY OF HUMAN PAPILLOMA VIRUS INFECTIONS

"A positive HPV test, especially in young women, rarely represents disease that could, if unrecognized, progress to cervical cancer."

"Knowing more about the natural history of HPV infection, especially in young women, reinforces the view that testing should *not* be carried out among women under age 35."

12-2 PERSISTENT HUMAN PAPILLOMAVIRUS INFECTION AS A PREDICTOR OF CERVICAL INTRAEPITHELIAL NEOPLASIA

The study adds to the body of evidence strongly implicating persistent HPV infections, particularly with oncogenic strains, as a cause of SIL.

"A strong relationship exists between *persistent* HPV infection and SIL incidence, especially for HPV types 16 and 18."

The study adds to the body of evidence strongly implicating persistent HPV infections, particularly with oncogenic strains, as a cause of SIL.

The investigators support the application of repeated type-specific HPV DNA testing in screening for SIL (and by implication prevention of cervical cancer). Vaccines against oncogenic strains (especially type 16 and 18) are a potential for prevention.

Practical point: Watch for developments. Is this the next major step in cancer prevention?

HYPERTENSION

1-3 LONG-TERM WEIGHT LOSS AND CHANGES IN BLOOD PRESSURE: Results of the Trials of Hypertension Prevention, Phase II

Clinically significant long-term reductions in BP and reduced risk of hypertension can be achieved with even modest weight loss (5% to 10%).

1-4 OBESITY AND HYPERTENSION: What Should We Do?

Americans have intense interest in losing weight. Huge sums are spent in the effort. Physician's advice may produce some benefit, but weight-loss advice is frequently not given. Even in motivated persons, the motivation gradually wanes and few continue the recommended calorie restriction and the exercise program. Weight control is a major unsolved problem in clinical medicine. Primary care clinicians should set an example for weight control and physical activity, and relentlessly encourage overweight patients to lose and maintain the loss.

1-5 EFFECTS ON BLOOD PRESSURE OF REDUCED DIETARY SODIUM AND THE DIETARY APPROACHES TO STOP HYPERTENSION (DASH) DIET

The DASH diet is rich in vegetables, fruits, and low-fat dairy products; low in meat. Adherence to the diet will decrease BP significantly in hypertensive persons as well as in those without hypertension. Adding salt restriction lowers BP still more. This has important implications for both prevention and treatment of hypertension.

1-6 ANTIHYPERTENSIVE DRUG THERAPIES AND RISK OF ISCHEMIC STROKE.

The study suggests a particular benefit of thiazide diuretics in reducing the risk of ischemic stroke.

Compared with those using beta-blockers alone, calcium blockers alone, or ACE inhibitors alone, users of a thiazide diuretic alone experienced a much lower incidence of ischemic stroke.

Among users of 2 drugs, those patients who received 2 drugs other than a thiazide had a 1.3 greater relative risk than those receiving a thiazide as one of the two.

The most recent (1997) report of the National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends diuretics as a first-line antihypertension agent.

4-3 ADVERSE DRUG EFFECTS, COMPLIANCE, AND INITIAL DOSES OF ANTIHYPERTENSIVE DRUGS RECOMMENDED BY THE JOINT NATIONAL COMMITTEE VS THE *PHYSICIANS' DESK REFERENCE*

The PDR does not reflect the lowest doses recommended for initiation of therapy for hypertension recommended by the JNC. Because avoidance of adverse drug reactions is essential in maintaining compliance, and because many ADEs are dose-related, physicians must use the very lowest, effective, least ADE-prone doses.

Practical point: It is basically important to start therapy with the lowest reasonable dose of drugs, especially drugs for long-term use. Most adverse effects are related to dosage. Starting low and slowly titrating up will avoid many adverse effects.

5-11 AUTOMATED SPHYGMOMANOMETRY: AMBULATORY BLOOD PRESSURE MEASUREMENT

Practical point: Due to the frequent occurrence of difficult-to-treat hypertension, all primary care practices should have some method of measuring ambulatory BP

5-12 WHAT TO DO WHEN BLOOD PRESSURE IS DIFFICULT TO CONTROL

In the majority of patietns treated for hypertension, target BP levels are not achieved.

Practical point: Primary care clinicians should consult a check-list of the reasons for inadequate control.

6-5 EFFECT OF RAMIPRIL VS AMLODIPINE IN RENAL OUTCOMES IN HYPERTENSIVE NEPHROSCLEROSIS

Practical point: African Americans with hypertension are at high risk of renal dysfunction. Obviously, do not wait for renal dysfunction to be established before beginning effective anti-hypertension therapy. We should protect the kidney as well as the heart and brain. Identifying and treating patients at the stage of microalbuminuria (20 to 200 mg/d) would lead to greater benefit than waiting for renal dysfunction to become established. Angiotensin converting enzyme inhibitors are the drugs of choice.

8-1 CHARACTERISTICS OF PATIENTS WITH UNCONTROLLED HYPERTENSION IN THE UNITED STATES

Most cases of uncontrolled hypertension consist of isolated systolic hypertension in older adults, most of whom have access to health care.

Treatment of systolic hypertension does not remove the cause. (Ie, does not improve compliance of large vessels.) This risk factor remains. Nevertheless, reducing the systolic load probably slows progression of the stiffening, and lowers risk of endothelial rupture and arterial thrombosis.

Practical point: Primary care clinicians have the opportunity and responsibility of diagnosing and treating systolic hypertension in their elderly patients. Treatment should begin low and continue slow. There is no urgency. It is most important to avoid adverse effects lest the patient become discouraged and discontinue treatment.

8-2 CONTROL OF HYPERTENSION — AN IMPORTANT NATIONAL PRIORITY

Epidemiologic data indicate that systolic BP is more important than diastolic as a determinant of cardiovascular risk. In patients with isolated systolic BP, antihypertensive therapy has been shown to reduce mortality and the incidence of stroke, myocardial infarction, and heart failure.

Practical point: The National Heart, Lung, and Blood Institute recommends that systolic BP become the major end point for the detection, evaluation, and treatment of hypertension. "Clearly, a shift needs to occur in clinical practice to focus more on the management of systolic rather than diastolic hypertension."

8-3 HORMONE REPLACEMENT THERAPY AND LONGITUDINAL CHANGES IN BLOOD PRESSURE IN POSTMENOPAUSAL WOMEN

Postmenopausal women taking HRT had a smaller increase in systolic BP over time than non-users. The difference increased with age.

Practical point: Primary care clinicians may consider this another mechanism for the protective effect of HRT. For those clinicians who believe the benefits of HRT outweigh the harms, another reason to prescribe it.

9-8 RANDOMIZED TRIAL OF A PERINDOPRIL-BASED BLOOD-PRESSURE-LOWERING REGIMEN AMONG 6105 INDIVIDUALS WITH PREVIOUS STROKE OR TRANSIENT ISCHAEMIC ATTACK.

In patients with previous stroke or TIA, a combination of an ACE inhibitor and a diuretic lowered mean BP from about 148/86 to about 125/75 and resulted in a large reduction in risk of recurrence of stroke.

"Treatment . . . should be considered routinely for patients with a history of stroke or TIA, irrespective of their BP."

Importantly, benefit for BP lowering was evident in patients not usually considered to be hypertensive — ie, those with "high normal" BP in whom BP was lowered from a mean of 136/79 to 127/75.

Practical point: A reduction to about 125/75 would benefit without causing harm.

10-1 CARDIOVASCULAR PROTECTION AND BLOOD PRESSURE REDUCTION: A Meta-Analysis

On average, all antihypertensive drugs have similar long-term efficacy and safety in providing cardiovascular protection.

Compared with diuretics and beta-blockers, calcium channel blockers might protect more against stroke and less against myocardial infarction. This results in an overall cardiovascular benefit similar to that of old classes of antihypertension drugs.

10-13 ELEVATED MIDLIFE BLOOD PRESSURE INCREASES RISK IN ELDERLY PERSONS: The Framingham Study

Elevated BP during the midlife decades contributes to the risk of stroke in older age. Optimal prevention of late-life stroke will likely require control of midlife BP.

Practical point: Hypertension should be controlled throughout life.

Archives Int Med October 22, 2001 pawolf@bu.edu Philip A Wolf

11-4 IMPACT OF HIGH-NORMAL BLOOD PRESSURE ON THE RISK OF CARDIO-VASCULAR DISEASE.

High normal BP (130-139/85-89) was associated with an increased risk of cardiovascular disease.

Practical point: Would not lowering "high normal" BP (130-139/85-89) in individuals at high risk due to a combination of factors seem reasonable? Certainly, life style measures are indicated. Drug therapy should be reserved for those with multiple risk factors, addressing all factors at the same time.

11-5 ASSESSMENT OF FREQUENCY OF PROGRESSION TO HYPERTENSION IN NON-HYPERTENSIVE PARTICIPANTS IN THE FRAMINGHAM HEART STUDY

Normal (120-129/80-85) and high normal (130-139/85-89) frequently progressed to hypertension >140/90) over 4 years, especially in older overweight adults. This supports the recommendation for monitoring those with high normal BP every year, those with normal BP every 2 years.

Control of weight and weight gain is important for primary prevention.

Practical point: regular screening for hypertension is a major responsibility of primary care clinicians. Weight control is also a major challenge. Development of systolic hypertension seems almost inevitable as age progresses. When to treat isolated systolic hypertension is another major challenge.

12-1 LEFT VENTRICULAR CHANGES IN ISOLATED OFFICE HYPERTENSION

Patients with isolated office ("white coat") hypertension had LV morpho-functional characteristics which differed significantly from normotensive patients and were qualitatively similar to subjects with sustained hypertension.

Isolated office hypertension should not be considered a benign condition.

12-16 BLOOD PRESSURE REDUCTION AND CARDIOVASCULAR RISK IN HOPE STUDY

The investigators concluded that ramipril confers substantial benefits *in addition* to those of other BP-lowering drugs. Benefit was greater than expected from the modest lowering of BP which occurred during the trial. But, is there really any benefit in reducing cardiovascular morbidity conferred by a drug in addition to its BP-lowering effect? Controversy remains.

Practical point: The first goal in treatment of hypertension by primary care clinicians should be lowering the BP to recommended levels -- combined by treatment of all risk factors in addition to the BP. (I believe that when this is accomplished, any particular drug used will have little additional benefit. However, There is increasing evidence of special benefits from ACE inhibitors and angiotensin II blocking agents. RTJ)

HYPOCHONDRIASIS

11-13 THE PATIENT WITH HYPOCHONDRIASIS

Although there is no definitive therapy, physicians can effectively care for patients with hypochondriasis by acknowledging that somatic symptoms without a medical basis can be as distressing as those resulting from demonstrable disease. The goal of treatment should be to improve coping with symptoms rather than their elimination, as in the management of chronic physical illness. This approach minimizes the frustration of both the patient and the physician.

Patients with hypochondriasis are a subgroup of patients who somatize — namely those whose medically unexplained symptoms are accompanied by an unshakable conviction that they have a serious disease. Overlap exists.

There is good evidence that vigorous treatment of psychiatric disorders that frequently co-exist are responsive to drugs. Drug treatment may help resolve hypochondriacal symptoms associated with major depression, panic disorder, and obsessive-compulsive disorder.

INDIGESTION

12-9 INDIGESTION: WHEN IS IT FUNCTIONAL?

Patients often complain of "indigestion". This may be defined differently by individual patients. To some it is heartburn and acid regurgitation; others may describe abdominal rumblings and belching; others, non-painful discomfort in the upper abdomen (fullness, bloating, early satiety).

"Dyspepsia" is best restricted to mean pain or discomfort centered in the upper abdomen.

There are many causes of dyspepsia. But, at least two thirds of patients have no structural or biochemical explanation for their symptoms.

It has been suggested that dyspepsia can be subdivided based on clusters of symptoms. But, subgroups have not proved to be of value in identifying the underlying cause. Symptoms overlap considerably.

Practical point: Perhaps asking patietns with troublesome dyspepsia to read this article may help them.

INFECTIOUS DISEASE

4-19 ANTIBIOTIC DATABASE LAUNCHED

Johns Hopkins has a free to all peer reviewed database presenting the latest information on antibiotics and infectious diseases. (www.hopkins-abxguide.org).

Practical point: This easily accessed website should be most helpful to primary care clinicians.

INFLUENZA

10-12 CONTRIBUTION OF INFLUENZA AND RESPIRATORY SYNCYTIAL VIRUS TO COMMUNITY CASES OF INFLUENZA-LIKE ILLNESS

In individuals with influenza-like illness, there is a substantial potential for confusion between illness caused by RSV and IV. In this study about 20% of adults with flu-like symptoms were positive for respiratory syncytial virus. RSV is an important pathogen contributing to the burden of illness in the entire community in winter.

Practical point: Watch for development of RSV vaccine for adults.

INFLUENZA VACCINE

11-7 THE SAFETY OF INACTIVATED INFLUENZA VACCINE IN ADULTS AND CHILDREN WITH ASTHMA.

"Influenza vaccine does not worsen asthma." Current guidelines for the immunization of patients with asthma are safe. In a large diverse group of adults and children with asthma, adverse effects were no more common in those receiving flu vaccine than in those receiving placebo injections.

Practical point: Health care providers should urge patients with asthma to be immunized and thus reduce the morbidity associated with influenza. Patients may be reassured by referring them to this study.

INSOMNIA

11-8 PYRAZOLOPYRIMIDINES

Zaleplon (*Sonata*) has many attributes of the ideal hypnotic agent — rapid absorption, rapid onset, adequate duration of action, minimum or no residual effect on daytime performance, and no evidence of pharmacological tolerance or withdrawal. "It provides another very helpful option in the management of patients with insomnia."

INTEGRATIVE MEDICINE

1-21 INTEGRATIVE MEDICINE: Orthodox Meets Alternative.

The January 20 issue of BMJ presented 8 articles on integrative (alternative; complementary) medicine. I abstracted a few highpoints. RTJ

JEHOVAH'S WITNESSES

1-19 BIOETHICAL ASPECTS OF THE RECENT CHANGES IN THE POLICY OF REFUSAL OF BLOOD BY JEHOVAH'S WITNESSES

The commentator concludes that if the act of receiving blood is kept strictly confidential and not made known to the religious community, expulsion is unlikely. Under the ideal protection of medical confidentiality, decisions on blood transfusion made by a patient who is a Jehovah's Witness would be known only to the patient and the medical team, not the congregation.

Probably the most important advice to doctors at this time of flux in the policy of refusal of blood is to treat individual patients independently of the church's official policy. "Each case needs to be discussed and treated individually."

LIFE STYLE

1-3 LONG-TERM WEIGHT LOSS AND CHANGES IN BLOOD PRESSURE: Results of the Trials of Hypertension Prevention, Phase II

Clinically significant long-term reductions in BP and reduced risk of hypertension can be achieved with even modest weight loss (5% to 10%).

1-5 EFFECTS ON BLOOD PRESSURE OF REDUCED DIETARY SODIUM AND THE DIETARY APPROACHES TO STOP HYPERTENSION (DASH) DIET

The DASH diet is rich in vegetables, fruits, and low-fat dairy products; low in meat. Adherence to the diet will decrease BP significantly in hypertensive persons as well as in those without hypertension. Adding salt restriction lowers BP still more. This has important implications for both prevention and treatment of hypertension.

1-17 INTAKE OF FISH AND OMEGA-3 FATTY ACIDS AND RISK OF STROKE IN WOMEN

Higher consumption of fish and omega-3 polyunsaturated fatty acids was associated with a reduced risk of thrombotic infarction, primarily among women who did not take aspirin regularly. No relation to hemorrhagic stroke.

5-2 PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

Type 2 diabetes can be prevented by changes in the lifestyle of patients with impaired glucose tolerance

Although the average amount of weight lost was not large, the difference between groups in incidence of diabetes was substantial. Even a relatively small loss of 5% of weight was important. The conservative target of more than 4 hours of exercise per week was associated with a significant reduction in risk. "The reasonably low dropout rate in our study indicates that subjects with impaired glucose tolerance are willing and able to participate in a demanding intervention program."

Practical point: This is an important study. Glucose metabolism should be checked in older patients. Discovery of moderate abnormalities (impaired fasting glucose and impaired glucose tolerance) will provide an excellent opportunity to encourage patients to modify their lifestyles.

6-3 THE EFFECT OF FRUIT AND VEGETABLE INTAKE ON RISK FOR CORONARY DISEASE

The data support a protective effect of greater consumption of fruits and vegetables, particularly green leafy vegetables and vitamin C rich fruits and vegetables, against CHD.

Practical point: Primary care clinicians should repeatedly advise patients about the benefits of a healthy diet.

6-14 SMOKING CESSATION AND THE COURSE OF MAJOR DEPRESSION

Smokers with a history of depression who abstained from smoking were at high risk of developing a new episode of major depression.

Practical point: How should primary care clinicians respond to this information? Which is worse -- continuing smoking or developing another episode of major depression? Is cigarette smoking always bad? Obviously, millions of persons choose to smoke fully knowing the risks. There must be some benefit. Relentlessly pushing some patients to stop smoking could drive them away. A frank discussion about pros and cons might lead to a trial of nicotine replacement.

6-21 FATTY FISH CONSUMPTION AND RISK OF PROSTATE CANCER.

Consumption of large amounts of fatty fish over years was associated with a decreased incidence of PC.

Practical point: Another possible benefit of fish. Primary care clinicians should recommend fish consumption in the healthy diet for protection against cardiovascular disease -- and now, possibly to protect against PC.

7-1 TEN YEARS OF LIFE

Life-style choices regarding diet, exercise, smoking, body weight, and hormone replacement singly and in combination appeared to lengthen life-expectancy by many years.

Practical point: Primary care clinicians should adopt these lifestyles themselves. Then they can encourage patients to do likewise. Publication of this study might motivate some patients.

7-10 A PROSPECTIVE STUDY OF PHYSICAL ACTIVITY AND COGNITIVE DECLINE IN ELDERLY WOMEN.

Elderly women with higher levels of baseline physical activity were less likely to develop cognitive decline over the next 6 to 8 years.

Practical point: Another point for clinicians to encourage fitness over a lifetime.

7-11 ACUTE EFFECTS OF PASSIVE SMOKING ON THE CORONARY CIRCULATION IN HEALTHY YOUNG ADULTS.

Passive smoking substantially reduced coronary blood flow reserve in healthy non-smokers. Passive smoking may cause endothelial dysfunction in the coronary circulation in non-smokers.

This should convince the diehards who still maintain that harms of passive smoking are not proven. It strengthens the resolve of those who oppose smoking in public places

9-1 DIET, LIFESTYLE, AND THE RISK OF TYPE 2 DIABETES MELLITUS IN WOMEN.

Most cases of type 2 diabetes could be prevented by a healthy lifestyle: weight control, regular exercise, modification of diet, abstinence from smoking, and limited consumption of alcohol.

Weight control would appear to offer the greatest benefit.

9-2 EFFECTS OF EXERCISE ON GLYCEMIC CONTROL AND BODY MASS INDEX IN TYPE 2 DIABETES MELLITUS

Exercise programs per se, both resistance and aerobic, over a 4 month period resulted in a reduction in HbA1c of a magnitude likely to be of clinical significance. .

Practical points:

A. Exercise improved HbA1c, not dependent on weight loss.

B. Resistance exercise was also of value, especially applicable to patients who cannot walk.

C. Patients can be told as little as 4 months of consistent exercise 3 to 4 times weekly will benefit.

D. Exercise per se is likely to be beneficial in preventing development of type 2 diabetes in patients with impaired glucose tolerance or elevated fasting glucose levels not now considered as having type 2 diabetes.

11-10 LEGUME CONSUMPTION AND RISK OF CORONARY HEART DISEASE IN US MEN AND WOMEN

A significant benefit in reducing incidence of cardiovascular disease was associated with increased legume consumption of at least 4 servings weekly.

LIPIDS

1-9 EARLY STATIN TREATMENT FOLLOWING MYOCARDIAL INFARCTION AND 1-YEAR SURVIVAL.

Early initiation of statin treatment in patients with acute MI was associated with reduced 1-year mortality. "Initiation of statin treatment before or at the time of hospital discharge should be recommended for all acute MI survivors with total cholesterol or low density cholesterol levels above current guideline levels for statin treatment as secondary prevention."

1-10 REVIEW OF FIRST 5 YEARS OF SCREENING FOR FAMILIAL HYPERCHOLESTEROLAEMIA IN THE NETHERLANDS.

Primary care clinicians will inevitably encounter patients with FHC. It is common and leads to premature cardiovascular disease and death. When an unselected patient is identified with an unusually high cholesterol (eg, > 275) the family members should be screened.

Family screening of index individuals with FHC is highly effective in identifying family members with FHC, and leads to effective prophylactic therapy.

4-7 EFFECTS OF ATORVASTATIN ON EARLY RECURRENT ISCHEMIC EVENTS IN ACUTE CORONARY SYNDROMES: The MIRACL Study

High dose atorvastatin started within 1 to 3 days after presentation for acute coronary syndromes was associated with a reduction in risk of early recurrent ischemic events, but with no other significant clinical benefit.

Practical point: Statin drugs given immediately after onset of acute myocardial infarction or unstable angina may be associated with only small benefits over 4 months. Nevertheless, statins should be started for secondary prevention and maintained over years. Starting early in the hospital will encourage compliance.

4-8 EFFECT OF LIPID-LOWERING THERAPY ON EARLY MORTALITY AFTER ACUTE CORONARY SYNDROMES.

Prescription of a lipid-controlling drug at hospital discharge for patients with unstable angina or MI, was independently associated with reduced short-term mortality over 1 month and 6 months.

Practical point: There is good reason for prescribing statin drugs to patients with acute coronary syndromes (ie, established coronary disease) during their hospitalization or at discharge.

5-1 EXECUTIVE SUMMARY OF THE THIRD REPORT OF THE NATIONAL CHOLESTEROL EDUCATION PROGRAM (NCEP) EXPERT PANEL ON DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD CHOLESTEROL IN ADULTS (Adult Treatment Panel III)

Practical point: All primary care clinicians should have a copy of these guidelines available for reference and distribution to patients with lipid problems. This will include millions.

5-8 BENEFITS OF PRAVASTATIN ON CARDIOVASCULAR EVENTS AND MORTALITY IN OLDER PATIENTS WITH CORONARY HEART DISEASE ARE EQUAL TO OR EXCEED THOSE SEEN IN YOUNGER PATIENTS: The LIPID Trial

Practical point: Older persons with established coronary disease and average or moderately elevated cholesterol levels may benefit from secondary prevention with pravastatin therapy. Co-morbidity, expected length of life, and personal preference are contraindications, not age

6-18 HIGH-DENSITY LIPOPROTEIN CHOLESTEROL AND ISCHEMIC STROKE IN THE ELDERLY: The Northern Manhattan Stroke Study

Increased HDL-c levels were associated with reduced risk of ischemic stroke in the elderly. This is possibly another benefit of statin drugs which raise HDL-c.

Practical point: Primary care clinicians should consider the entire lipid profile, not just the total cholesterol or the LDL-cholesterol, when advising patients about risks.

9-11 BLOOD LIPID CONCENTRATIONS AND RISK OF MYOCARDIAL INFARCTION

As in the West, Algerians who survived a MI, had higher total cholesterol and LDL-cholesterol, and lower HDL-cholesterol than controls. However, concentrations rarely reached the levels usually considered when instituting treatment in Western countries. The ratio of total-c/HDL-c, and of
LDL-c/HDL-c, as in the West were similarly elevated. These ratios are therefore good predictors of risk, irrespective of nationality.

Practical point: A ratio has greater predictive value than total-cholesterol or LDL-cholesterol alone. Total cholesterol levels alone may be very misleading.

11-6 SIMVASTATIN AND NIACIN, ANTIOXIDANT VITAMINS, OR THE COMBINATION FOR THE PREVENTION OF CORONARY DISEASE.

Compared with placebo, combined niacin-statin (simvastatin) provided marked clinical and angiographic benefits in patients with established coronary disease and low HDL levels. (Secondary prevention). The decrease in LDL related to combined statin-niacin was greater than the average decrease reported from statin therapy alone. The increase in HDL was much more than usually reported from statins alone. The rate of major clinical events was reduced by 90% in the simvastatin + niacin group.

Antioxidants did not benefit. "Unless more compelling evidence appears, we see little justification for
the use of antioxidant vitamins for the prevention of cardiovascular events."

12-7 TOTAL CHOLESTEROL/HDL-CHOLESTEROL RATIO VS LDL-CHOLESTEROL/HDL-CHOLESTEROL RATIO AS INDICES OF ISCHEMIC HEART RISK IN MEN

In addition to the well-established conventional risk factors, the Total-c/HDL-c ratio may represent an important cumulative index of the presence of an atherogenic dyslipidemic profile associated with insulin resistance.

It was a simple index of IHD risk in men in this study.

Calculation of the LDL-c/HDL-c ratio may underestimate IHD risk in some patients since it ignores any contribution of the cholesterol in triglycerides.

Practical point: This may be a valid alternative to risk assessment. Calculation or determination of LDL-c may be eliminated, making assessment simpler.

12-8 FREQUENCY OF EATING AND CONCENTRATIONS OF SERUM CHOLESTEROL

In a general population, concentrations of total cholesterol and LDL cholesterol were decreased consistently by increased frequency of eating. "We need to consider not just what we eat, but how often we eat."

Practical point: Nibbling may be healthy; gorging unhealthy. It makes sense not to stress your metabolic machinery.

LYME DISEASE

7-19 PROPHYLAXIS WITH SINGLE-DOSE DOXYCYCLINE FOR THE PREVENTION OF LYME DISEASE AFTER AN *IXODES SCAPULARIS* TICK BITE

A single dose of doxycycline given within 3 days of a recognized tick bite prevented development of Lyme disease.

Who should receive prophylactic doxycycline?

Persons bitten by ticks in endemic areas.

The tick is at least partially engorged.

The tick is a nymphal deer tick.

Practical point: This applies to only a few primary care clinicians. The application is important to them and their patients.

MACULAR DEGENERATION

8-8 RISK OF MACULAR DEGENERATION IN USERS OF STATINS

An exciting, but preliminary report of considerable lowering of risk of macular degeneration in older persons taking statin drugs.

11-9 ANTIOXIDANTS AND ZINC TO PREVENT PROGRESSION OF AGE-RELATED MACULAR DEGENERATION

Persons older than 55 years should have dilated eye examinations to determine the risk of developing advanced ARMD.

Practical point: Those with extensive intermediate size drusen, at least one large druse, non-central geographic atrophy in one or both eyes, or advanced ARMD or vision loss, and without contraindications such as smoking (which may increase adverse effects of beta carotene) should consider taking a supplement of antioxidants plus zinc such as used in this study.

MEDICAL DECISION MAKING

12-12 ENGAGING PATIENTS IN MEDICAL DECISION MAKING

Three questions dominate the debate about the role of the patient in making treatment decisions:

Can patients take a leading role in making decisions?

Do they want to?

What if doctors and public health professionals don't like their choices?

Fully informed shared decision making is difficult to conduct in practice. Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal. "Most patients want to see the road map, including alternative routes, even if they don't want to take the wheel."

Fully informed shared decision making is difficult to conduct in practice.

Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal.

Practical point: Determining how much patients wish to be involved is a good start.

MENINGOCOCCAL DISEASE

5-14 MENINGOCOCCAL DISEASE

A review. Smoking and inhaling smoke may predispose to meningococcemia.

Practical point: Primary care clinicians should be prepared to administer antibiotics empirically to sick patients suspected of meningococcemia. Delay increases mortality.

MIGRAINE

1-18 PROPHYLACTIC TREATMENT OF MIGRAINE WITH ANGIOTENSIN CONVERTING ENZYME INHIBITOR (LISINOPRIL)

The ACE-inhibitor lisinopril had a clinically important prophylactic effect in migraine.

MYOCARDIAL INFARCTION

1-9 EARLY STATIN TREATMENT FOLLOWING MYOCARDIAL INFARCTION AND 1-YEAR SURVIVAL.

Early initiation of statin treatment in patients with acute MI was associated with reduced 1-year mortality. "Initiation of statin treatment before or at the time of hospital discharge should be recommended for all acute MI survivors with total cholesterol or low density cholesterol levels above current guideline levels for statin treatment as secondary prevention."

4-5 PRIOR ALCOHOL CONSUMPTION AND MORTALITY FOLLOWING MYOCARDIAL INFARCTION

Moderate alcohol consumption in the year prior to an acute MI was associated with reduced mortality following infarction.

Practical point: What should we advise abstainers when discharged from the hospital following an acute MI? The number needed to treat (among those using alcohol in the year prior to the MI) to benefit one patient is comparable to other pharmacotherapeutic interventions. I believe some competent stable patients and their families should be informed of the likely (but not proven) benefits of one drink a day.

They may then choose for themselves. Just as for any drug, a prescription for "A cocktail before dinner (1 oz spirits), or a glass of wine (4 oz) with dinner — not both" may be written. Individuals who do drink moderately and develop left ventricular dysfunction, heart failure, or other effects of CHD generally should *not* be told to discontinue consumption.

5-6 EFFECT OF CARVEDILOL ON OUTCOME AFTER MYOCARDIAL INFARCTION IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION: THE CAPRICORN RANDOMISED TRIAL.

In patients treated long-term after an acute MI complicated by left ventricular systolic dysfunction. carvedilol,a beta-blocker, started within days after the MI, was associated with reduction in all-cause and cardiovascular mortality, and recurrent non-fatal MI. Benefits were in addition to aspirin and ACE inhibitors.

Practical point: Primary care clinicians will be following more patients taking beta-blockers. Starting low and going slow is a critical clinical application.

6-2 OPTIMAL TREATMENT OF ACUTE CORONARY SYNDROMES — An Evolving Strategy

This article summarizes the latest recommendations. A reference algorithm is presented on p 1941.

Practical point: Primary care clinicians can serve their patients optimally by immediately beginning non-interventional measures (aspirin, heparin, oral beta-blocker, and medication for pain control). Primary care clinicians remote from emergency centers must keep up with the rapid changes in therapy in order to correlate urgent treatment with their cardiologist colleagues. Each minute of myocardial ischemia adds to risk. The new bolus agents will facilitate early fibrinolysis out of hospital.

6-16 DO DOCTORS POSITION DEFIBRILLATION PADDLES CORRECTLY?

The International Liaison Committee of Resuscitation guidelines specify placement of the centers of the two paddles:

Sternal paddle — below the **right** clavicle in the mid-clavicular line

Apical paddle — to the left of the nipple with the center of the electrode in the mid-axillary line.

7-2 BOLUS FIBRINOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION

Given the ease of administration and the similar outcomes compared with recombinant tPA, it is likely that a key component of reperfusion will include a bolus fibrinolytic. The simple bolus administration should shorten the time between onset of symptoms and treatment (onset-to-needle time). It should facilitate pre-hospital fibrinolysis and improve prognosis.

Practical point: Primary care clinicians who do not have immediate access to emergency department consultations should be able to administer the newer bolus fibrinolytics in the office.

8-5 EFFICACY AND SAFETY OF TENECTEPLASE IN COMBINATION WITH ENOXAPARIN, ABCIXIMAB, OR UNFRACTIONATED HEPARIN: The ASSENT-3 Randomised Trial in Acute Myocardial Infarction

Tenecteplase is a new genetically engineered variant of alteplase (tPA; tissue plasminogen activator). It provides a new standard of fibrinolytic therapy by virtue of its equivalent efficacy with regard to 30-day mortality, its reduced propensity for bleeding complications, and its simple administration as a bolus.

“In view of the present data and the ease of administration, enoxaparin might be regarded an attractive alternative anticoagulant given in combination with tenecteplase.”

Taking into account efficacy and safety, the combination of full-dose bolus tenecteplase + enoxaparin for 7 days emerged as the best treatment in this trial. Because of ease of administration and the lack of monitoring of anticoagulation, this combination should be regarded as an attractive alternative pharmacological reperfusion strategy deserving further study.

Practical point: Primary care clinicians will soon have the opportunity and responsibility to apply immediate (bolus) out-of-hospital thrombolysis.

9-11 BLOOD LIPID CONCENTRATIONS AND RISK OF MYOCARDIAL INFARCTION

As in the West, Algerians who survived a MI, had higher total cholesterol and LDL-cholesterol, and lower HDL-cholesterol than controls. However, concentrations rarely reached the levels usually considered when instituting treatment in Western countries. The ratio of total-c/HDL-c, and of
LDL-c/HDL-c, as in the West were similarly elevated. These ratios are therefore good predictors of risk, irrespective of nationality.

Practical point: A ratio has greater predictive value than total-cholesterol or LDL-cholesterol alone. Total cholesterol levels alone may be very misleading.

10-10 PROGNOSTIC VALUE OF A NORMAL OR NONSPECIFIC ELECTROCARDIOGRAM IN ACUTE MYOCARDIAL INFARCTION

In a large cohort of hospitalized patients with eventually established acute MI, those presenting with an initially normal or non-specific ECG had lower in-hospital mortality than those with initially diagnostic ECGs. However, absolute rates of mortality and complications were unexpectedly high.

Practical point: Among patients presenting with suspected acute MI, some will be discharged home without a proper diagnosis. Although they are relatively few, the consequences may be disastrous. These patients should be rechecked the next day even though the clinician feels the risk of MI is small. It would be reasonable to routinely give these patients prophylactic aspirin and even low-dose beta-blockers before discharge home.

10-11 FAST DIAGNOSIS OF MYOCARDIAL INFARCTION

A new test procedure now approved by the FDA simultaneously measures 3 cardiac markers: troponin I, creatine kinase-MB, and myoglobin. All are released by the damaged myocardium.

It can be performed quickly at the bedside. It is very predictive in ruling out acute MI.

11-15 A SIMPLE RISK INDEX FOR RAPID INITIAL TRIAGE OF PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

A simple risk index based on age, heart rate, and systolic BP captured most of the information from more complex tools. Risk rose sharply after age 60, after a pulse rate of 80, and when systolic BP fell below 120. The index is likely to be useful in rapid triage of patients with ST-elevation acute MI.

Practical point: This assessment could be a useful indicator for immediate use of a new bolus fibrinolytic agent at the primary encounter site.

NARRATIVE MEDICINE (See also DOCTOR-PATIENT RELATION; PATIENT-CENTERED MEDICINE

6-1 "TELL ME ABOUT YOURSELF": The Patient-Centered Interview.

Physicians should focus more attention on patient's concerns, feelings, and ideas. Inattention to the person of the patient, to the patient's characteristics and concerns, leads to inadequate clinical data-gathering, non-adherence, and poor outcomes. Each patient's experience of illness is unique. "To know what kind of a person has a disease is as essential as knowing what kind of disease a person has." The art (of listening) is long; time is short.

Practical point: Primary care physicians must go beyond disease-centeredness in the clinical encounter. They must become expert at listening without interruption and with undivided attention, and then lead patients to disclose more about themselves. RTJ

10-7 NARRATIVE MEDICINE

Narrative competence is the competence that human beings use to absorb, interpret, and respond to stories others tell. Everyone has a story to tell. Along with scientific ability, physicians need the ability to listen to the narratives of the patient, grasp and honor their meaning, and be moved to act on the patient's behalf.

NATRIURETIC PEPTIDE

10-14 THE PROGNOSTIC VALUE OF B-TYPE NATRIURETIC PEPTIDE IN PATIENTS WITH ACUTE CORONARY SYNDROMES.

A single measurement of BNP obtained within a few days of onset of ischemic symptoms provided powerful risk-stratification information across the entire spectrum of acute coronary syndromes.

It predicted long term risk of death and non-fatal coronary events. The prognostic usefulness persisted after adjustment for the presence of HF and other important predictors of mortality.

The authors suggest — B-type natriuretic peptide should be measured after an acute coronary syndrome in order to identify the risk of adverse outcomes. Treatment should be adjusted accordingly.

Practical point: Primary care clinicians should keep this marker in mind. It has not yet reached frequent clinical application, but probably will in the near future.

10-16 CONGESTIVE HEART FAILURE TREATMENT

The FDA has approved nesiritide (*Natrecor*), a preparation of human B-type natriuretic peptide, for intravenous treatment of acutely decompensated congestive heart failure (ADCHF).

OBESITY

1-3 LONG-TERM WEIGHT LOSS AND CHANGES IN BLOOD PRESSURE: Results of the Trials of Hypertension Prevention, Phase II

Clinically significant long-term reductions in BP and reduced risk of hypertension can be achieved with even modest weight loss (5% to 10%).

1-4 OBESITY AND HYPERTENSION: What Should We Do?

Americans have intense interest in losing weight. Huge sums are spent in the effort. Physician's advice may produce some benefit, but weight-loss advice is frequently not given. Even in motivated persons, the motivation gradually wanes and few continue the recommended calorie restriction and the exercise program. Weight control is a major unsolved problem in clinical medicine. Primary care clinicians should set an example for weight control and physical activity, and relentlessly encourage overweight patients to lose and maintain the loss.

6-6 DRUG TREATMENT FOR OBESITY

The editorialist comments on a recent study of sibutramine which reported benefit in reducing weight re-gain after a program of weight loss.

Practical point: Should primary care clinicians prescribe sibutramine, or any other weight-loss drug? I would vote against it. I believe use should be limited to special clinics where suitable candidates can be carefully screened and followed. The adverse effect on BP is a serious downside.

9-13 LONG-TERM WEIGHT LOSS WITH SIBUTRAMINE

Sibutramine administered for 48 weeks resulted in clinically relevant weight loss compared with placebo.

Practical point: Although possibly of long term benefit, this therapy should be left to specialists.

OMEGA-3 FATTY ACIDS

1-17 INTAKE OF FISH AND OMEGA-3 FATTY ACIDS AND RISK OF STROKE IN WOMEN

Higher consumption of fish and omega-3 polyunsaturated fatty acids was associated with a reduced risk of thrombotic infarction, primarily among women who did not take aspirin regularly. No relation to hemorrhagic stroke.

OPIATE OVERDOSE

4-18 TAKE HOME NALOXONE AND THE PREVENTION OF DEATHS FROM OPIATE OVERDOSE

Practical point: Naloxone, a rapidly acting opioid antagonist will save lives of the opioid abusers who overdose. It

should be given routinely, on request, to all abusers.

We cannot abandon compassionate care of those who cannot or will not care for themselves.

OSTEOARTHRITIS

1-7 LONG-TERM EFFECTS OF GLUCOSAMINE SULPHATE ON OSTEOARTHRITIS PROGRESSION

Over 3 years, the combined structure-modifying and symptom-modifying effects of glucosamine sulphate suggest that it could be a *disease-modifying* agent in OA.

1-8 GLUCOSAMINE FOR OSTEOARTHRITIS: Dawn of a New Era?

Recent studies have shown that a pure form of oral glucosamine sulfate has anti-inflammatory and anabolic properties on arthritic joints. A robust mechanistic explanation is lacking.

The drug is widely available in the US as a nutritional supplement. Since it is generally self-prescribed, the results may not be generalizable due to the highly variable formulations of nutritional products bought off the counter.

6-19 GLUCOSAMINE FOR OSTEOARTHRITIS: Magic, Hype, or Confusion?

"We conclude that there is more confusion and hype than magic about glucosamine. The rationale for its use in unclear; the best dose and route of administration are unknown, and the published trials do not allow any conclusion about its efficacy or cost effectiveness. However, it seems to be safe.

Practical point: When patients confront primary care clinicians about use of glucosamine, how should they respond? I would neither prescribe it nor dissuade patients who are convinced of its benefit from taking it since it appears to be safe.

OSTEOPOROSIS

4-16 RISK OF FRACTURE IN WOMEN WITH LOW SERUM LEVELS OF THYROID-STIMULATING HORMONE

Older women with biochemical evidence of physiological hyperthyroidism (low TSH), mainly due to too high doses of exogenous thyroxine, but also due to endogenous "subclinical hyperthyroidism", had an increased risk of hip and vertebral fracture.

Practical point: Consider any woman with evidence of excess thyroid hormone production or administration at risk of increased severity of osteoporosis. Exogenous thyroxine dosage must be carefully monitored.

5-19 EFFECT OF PARATHYROID HORMONE (1-34) ON FRACTURES AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

Practical point: Primary care clinicians should be aware of this possibly beneficial advance. Look for general release and further information.

8-11 BONE MINERAL DENSITY RESPONSE TO ESTROGEN REPLACEMENT IN FRAIL ELDERLY WOMEN

In physically frail women, mean age 82, 9 months of HRT significantly increased BMD.

Traditional thought has been that the estrogen-dependent compartment of bone becomes depleted approximately 15 years after menopause. This concept has been challenged by those who believe that estrogen deficiency is also primarily responsible for the continuing decline in BMD that previously had been attributed to aging.

It was once commonly believed that bone turnover remained elevated for only a few years after menopause and that bone loss subsequently slowed or ceased in older women. Recent studies provide evidence that bone turnover remains elevated into old age and that bone loss may accelerate rather than slow in the elderly. (Subjects in this study had high rates of bone turnover as indicated by serum and urine markers.)

Practical point; Primary care clinicians should inform their elderly female patients of the possibility that bone sparing therapy is effective regardless of age, and allow them to make an informed choice to accept or reject.

10-4 GAIN IN BONE MINERAL MASS IN PREPUBERTAL GIRLS 3-5 YEARS AFTER DISCONTINUATION OF CALCIUM SUPPLEMENTATION.

Calcium supplementation during childhood and adolescence increases bone mass. Peak bone mass at the end of the prepubertal period is a major determinant of risk of osteoporotic fractures in later life.

Practical point: Primary care clinicians should make sure their adolescent girl patients receive adequate intake of calcium and vitamin D. Supplementation is often needed.

12-13 IDENTIFICATION AND FRACTURE OUTCOMES OF UNDIAGNOSED LOW BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN.

About half of a large screened population of postmenopausal women had previously undetected low BMD. Determination of low BMD at peripheral sites (distal radius, heel, finger), as well as at hip and spine, was highly predictive of fracture risk.

Given the economic and social costs of osteoporotic fractures, strategies to identify and manage osteoporosis in the primary care setting need to be established.

Practical point: Some adverse conditions are almost inevitable as age progresses. This includes postmenopausal osteoporosis, atherosclerosis, isolated systolic BP (due to loss of arterial elasticity), and weight gain. Should we wait for confirmatory tests to determine their presence? If so, opportunities for prevention are lost. Or should we assume that preventive measures for these almost universal risks should be started at the earliest reasonable time. Much expense and better prevention would result from empirical and universal primary interventions.

PAIN

4-15 UNDERSTANDING THE EXPERIENCE OF PAIN IN TERMINALLY ILL PATIENTS

Although half of terminally ill patients experience moderate to severe pain, only 30% of these wanted additional pain treatment. The number of patients experiencing pain remains too high, but the number is not as large as perceived.

Many patients are willing to tolerate pain for fear of addiction; dislike of mental or physical side effects; not wanting to take more pills or injections. Physicians must communicate more effectively that addiction to opioids given for pain relief is a myth.

Practical point: As usual, pain control as well as other aspects of treatment must be negotiated , and concordance reached, with each individual patient.

5-4 ENDOGENOUS OPIOIDS, PLACEBO RESPONSE, AND PAIN

It was suggested as early as 1978 that the analgesic response to placebo is mediated by endogenous opioids. Well designed studies have shown clearly that the placebo response to pain exists and that endogenous opioids have an important role in its mediation.

Practical point: The placebo response is physiological and mediated by endogenous opioids – a system which can provide pain relief. It is wrong to assume, as many clinicians still do, that a placebo response represents imagined pain or malingering.

5-16 RANDOMISED CROSSOVER TRIAL OF TRANSDERMAL FENTANYL AND SUSTAINED RELEASE ORAL MORPHINE FOR TREATING NON-CANCER PAIN

Patients with chronic non-cancer pain preferred transdermal fentanyl over oral sustained release morphine. Fentanyl provided better pain relief with less constipation, and an enhanced quality of life.

Practical point: Primary care clinicians must be able to provide adequate pain relief to patients with chronic pain, especially terminal patients. Fentanyl may be a good choice.

5-17 OPIOIDS IN CHRONIC NON-MALIGNANT PAIN

"The use of opioids in chronic non-malignant pain is profoundly messy. A simple start is to say that if somebody has severe pain which responds to opioids, and for which there is no other effective remedy, then why should they not receive opioids?" Two judgements are then implicit: 1) that opioids are effective, and 2) that other remedies are not.

"There is no evidence base on which we can rely other than common sense, our own experience, and that of others."

Practical point: A trial of opioids beckons only when the many other conventional pain treatments have been tried. It should not be withheld for fear of addiction in sick patients with chronic pain.

PANIC DISORDER

7-18 A 28-YEAR OLD WITH PANIC DISORDER

A clinical review article defining panic attack and panic disorder. Comments on diagnosis and treatment. "The cause is not known, but treatment is almost always successful."

PATIENT CENTERED MEDICINE (See also DOCTOR-PATIENT RELATIONSHIP; NARRATIVE MEDICINE)

4-15 UNDERSTANDING THE EXPERIENCE OF PAIN IN TERMINALLY ILL PATIENTS

Although half of terminally ill patients experience moderate to severe pain, only 30% of these wanted additional pain treatment. The number of patients experiencing pain remains too high, but the number is not as large as perceived.

Many patients are willing to tolerate pain for fear of addiction; dislike of mental or physical side effects; not wanting to take more pills or injections. Physicians must communicate more effectively that addiction to opioids given for pain relief is a myth.

Practical point: As usual, pain control as well as other aspects of treatment must be negotiated , and concordance reached, with each individual patient.

6-1 "TELL ME ABOUT YOURSELF": The Patient-Centered Interview.

Physicians should focus more attention on patient's concerns, feelings, and ideas. Inattention to the person of the patient, to the patient's characteristics and concerns, leads to inadequate clinical data-gathering, non-adherence, and poor outcomes. Each patient's experience of illness is unique. "To know what kind of a person has a disease is as essential as knowing what kind of disease a person has." The art (of listening) is long; time is short.

Practical point: Primary care physicians must go beyond disease-centeredness in the clinical encounter. They must become expert at listening without interruption and with undivided attention, and then lead patients to disclose more about themselves.
RTJ

10-7 NARRATIVE MEDICINE

Narrative competence is the competence that human beings use to absorb, interpret, and respond to stories others tell. Everyone has a story to tell. Along with scientific ability, physicians need the ability to listen to the narratives of the patient, grasp and honor their meaning, and be moved to act on the patient's behalf.

10-9 OBSERVATIONAL STUDY OF EFFECT OF PATIENT CENTEREDNESS AND POSITIVE APPROACH ON OUTCOMES OF GENERAL PRACTICE CONSULTATIONS.

Patient-centered approach includes five components.

1) Communication and partnership with the doctor.
2) Personal relationship with the doctor.
3) Health promotion.
4) Positive approach to diagnosis and prognosis.
5) Interest in the effect of the illness on the patient's life.

If the doctor provides a positive patient-centered approach, patients will be more satisfied, more enabled, and may have less symptom burden and fewer rates of referral.

12-12 ENGAGING PATIENTS IN MEDICAL DECISION MAKING

Three questions dominate the debate about the role of the patient in making treatment decisions:

Can patients take a leading role in making decisions?

Do they want to?

What if doctors and public health professionals don't like their choices?

Fully informed shared decision making is difficult to conduct in practice. Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal. "Most patients want to see the road map, including alternative routes, even if they don't want to take the wheel."

Fully informed shared decision making is difficult to conduct in practice.

Not all patients want to make their own decisions. Many want to delegate responsibility to their doctors. Yet a desire for information is nearly universal.

Practical point: Determining how much patients wish to be involved is a good start.

PERIPHERAL ARTERIAL DISEASE

5-5 MEDICAL TREATMENT OF PERIPHERAL ARTERIAL DISEASE AND CLAUDICATION

Peripheral atherosclerotic disease is an important manifestation of systemic atherosclerosis. It carries the same relative risk of death from cardiovascular disease as does a history of coronary heart disease or cerebrovascular disease.

Practical point; Patients with PAD should be candidates for secondary prevention strategies, including aggressive risk factor modification and antiplatelet drug therapy. Most patients are undertreated. The FDA has approved cilostazol (*Pletal*) for treatment of claudication. It inhibits platelet aggregation, arterial thrombus formation, and vascular smooth-muscle proliferation, and causes vasodilation.

9-4 PERIPHERAL ARTERIAL DISEASE DETECTION, AWARENESS, AND TREATMENT IN PRIMARY CARE.

PAD is prevalent in older Americans. It is associated with a high risk of cardiovascular complications. Many patients are not diagnosed before occurrence of a morbid event.

PAD is easily detected with the ankle/brachial index (ABI) in primary care.

Treatment of hypertension, lipid disorders, and diabetes are as important in patients with PAD as in patients with coronary disease. Smoking cessation is essential.

Practical point: Should all primary care clinicians make ABI available? Yes, but nor necessarily in their own offices. But, primary care clinicians should institute preventive measures far before the ABI becomes abnormal.

PHYSICIAN'S HEALTH

9-6 CHALLENGE OF CULTURE, CONSCIENCE, AND CONTRACT TO GENERAL PRACTITIONER'S CARE OF THEIR OWN HEALTH: Qualitative Study

Doctors perceive that their professional position and training adversely influence their attitudes to illness in themselves and their colleagues..

The list of doctor's duties begins with "make the care of your patient your first concern". The authors of this study suggest that a duty of self knowledge and self care should underpin this. Organizational changes within practice must take account of the barriers experienced in accessing physician health care. Medical education and culture should strive to promote appropriate self care among doctors.

Practical point: "Physician, heal thyself."

PHYSICIAN'S PRAYER

12-18 GOOD LORD, DELIVER US

"From the inability to let well enough alone; from too much zeal for the new and contempt for what is old; for putting knowledge above wisdom, science before art, and cleverness above common sense; from treating patients as cases; and from making the cure of the disease more grievous than the endurance of the same; Good Lord, deliver us"

Practical point: Amen

PLACEBO

5-3 IS THE PLACEBO POWERLESS?

An Analysis of Clinical Trials Comparing Placebo with No Treatment

This investigation concludes that placebo response represents a regression of symptoms to the mean and not a true therapeutic effect.

Practical point: Primary care clinicians must decide whether to 1) accept the possibility that placebos do indeed have a beneficial effect some times, for some patients. or 2) to believe they have no beneficial effect whatsoever, and avoid their use. Most clinicians will still tilt toward 1).

5-4 ENDOGENOUS OPIOIDS, PLACEBO RESPONSE, AND PAIN

It was suggested as early as 1978 that the analgesic response to placebo is mediated by endogenous opioids. Well designed studies have shown clearly that the placebo response to pain exists and that endogenous opioids have an important role in its mediation.

Practical point: The placebo response is physiological and mediated by endogenous opioids – a system which can provide pain relief. It is wrong to assume, as many clinicians still do, that a placebo response represents imagined pain or malingering.

POSTTRAUMATIC STRESS DISORDER

8-14 RECOGNITION AND TREATMENT OF POSTTRAUMATIC STRESS DISORDER.

PTSD is a worldwide problem which is reaching alarming proportions. It is associated with persistent disability and comorbidity. Treatment can produce a meaningful reduction in distress. The condition must first be recognized.

Practical point: Primary care clinicians will be seeing more patients with PTSD. Certainly they can elicit patient's experiences and feelings and listen empathetically. Compassionate understanding and treatment with selective serotonin reuptake inhibitors will benefit. There is no reason PTSD cannot be treated effectively in primary care.

POTASSIUM

9-10 BENEFICIAL EFFECTS OF POTASSIUM: Clinical Review

There is good evidence that potassium (K) intake is important in regulating blood pressure. Increasing K intake lowers BP in both hypertensive and normotensive patients.

This review article discusses other probable benefits of increased K intake: Lowering risk of stroke; prevention of renal vascular, glomerular, and tubular damage; reduction of urinary calcium excretion, possibly reducing stone formation and preventing bone demineralization; and reduction in risk of ventricular arrhythmias in patients with ischemic heart disease, heart failure, and left ventricular hypertrophy.

Practical point: The best way to increase K intake is to eat more fresh fruit and vegetables.

PROFESSIONALISM

12-17 PHYSICIAN CHARTER OF PROFESSIONALISM

A campaign to shore up physicians' special place in society has resulted in a *Charter of Professionalism.* The charter reminds physicians that satisfying in full the expectations of a medical professional is still within their control. Physicians may lead a full and satisfying life of medicine.

The Physician Charter of Professionalism contains three fundamental principles:

Primacy of patient welfare

Patient autonomy

Social justice

PROSTATE CANCER

5-9 PROSTATE-SPECIFIC-ANTIGEN TESTING FOR EARLY DETECTION OF PROSTATE CANCER

PSA testing does detect PC at an early age in many cases. However, at present, data are not available from large, well-designed, randomized trials to determine whether early detection is beneficial, harmful, or has no effects. As a result, the optimal strategy remains unknown.

A discussion about testing should include: the likelihood that PC will be diagnosed; the possibility of false positive and false negative tests; the anxiety associated with a positive test; and the uncertainty regarding whether screening reduces the risk of death from PC. Randomized trials have indicated that routinely providing such information reduces the proportion of men who elect to be tested, although many still elect to do so.

Practical point: Primary care clinicians should not automatically order a PSA screen on their male patients over age 50. They should first make sure the patient has enough understanding of adverse effects of possible follow-up procedures and surgery (or radiation) in order to make an informed decision about screening.

6-21 FATTY FISH CONSUMPTION AND RISK OF PROSTATE CANCER.

Consumption of large amounts of fatty fish over years was associated with a decreased incidence of PC.

Practical point: Another possible benefit of fish. Primary care clinicians should recommend fish consumption in the healthy diet for protection against cardiovascular disease -- and now, possibly to protect against PC.

PSORIASIS

6-17 EFFICACY AND SAFETY OF INFLIXIMAB MONOTHERAPY FOR PLAQUE-TYPE PSORIASIS

Patients with moderate to severe psoriasis receiving infliximab (an antibody to tumor necrosis factor) experienced a high degree of clinical benefit and rapid time to response. Tumor necrosis factor has a pivotal role in the pathogenesis of psoriasis.

Practical point: Primary care clinicians should establish a referral relationship with dermatologists who will be able to offer new treatments which will more safely and effectively reduce the severe physical and psychological effects psoriasis brings to many individuals.

PUBMED CENTRAL

1-20 PUBMED CENTRAL: http://pubmedcentral.nih.gov

This new web based repository will archive, organize, and distribute peer reviewed reports from biomedical journals. It promises to archive the full texts and make them available in perpetuity. It is funded by the US National Institutes of Health and the National Library of Medicine.

But, too much information is the bane of a working clinician's existence. Physicians, and ultimately the public do not need more articles. Instead, they need better articles, preferably from a trusted source, that give new and useful information or help put knowledge into some sort of practical context.

PULMONARY EMBOLISM

9-18 SEVERE PULMONARY EMBOLISM ASSOCIATED WITH AIR TRAVEL

The greater the distance and time traveled in airflights the greater the risk. The absolute incidence is low.

Almost all patients had high and moderate risk of thromboembolic disease.

The sitting position is associated with venous stasis. The double 90-degree angle bends at the knee and hip impede flow.

Practical point: Simple behavioral and mechanical prophylaxis should be considered to prevent air-travel associated PE and DVT, especially in patients with risk factors.

RACIAL PROFILING

5-21 RACIAL PROFILING IN MEDICAL RESEARCH

This editorialist maintains that attributing differences in a biological endpoint to race is not only imprecise, but also of no proven value in treating an individual patient.

Race is a social construct, not a scientific classification.

Sadly, the idea of race remains ingrained in clinical medicine. On ward rounds, it is routine to refer to a patient as “black”, “white”, or “Hispanic”. Yet these vague epithets lack medical relevance.

Practical point: The editorialist has a valid moral point, but not a practical clinical application. Race still plays an important role in determining pretest probabilities.

RENAL DISEASE

4-11 HAEMATURIA IN ASYMPTOMATIC INDIVIDUALS

Hematuria is often detected incidentally by “dipstick”. It is common. Should hematuria in asymptomatic individuals always be investigated or should it be disregarded?

In most cases the next step is to examine the urine by phase contrast microscopy to confirm the hematuria and to determine whether the red cells have originated from the glomerulus or elsewhere in the urinary tract. “Dysmorphic” or “glomerular” red cells are present when there is glomerulonephritis with proliferative features. “Non-glomerular” red cells appear when the bleeding comes from elsewhere in the urinary tract – usually infections, stones, or a tumor.

Renal biopsy most often shows "*thin basement membrane disease*". Prognosis is excellent.

Practical point: Primary care clinicians should be aware of this entity. It may save patients much anxiety and useless investigations

6-5 EFFECT OF RAMIPRIL VS AMLODIPINE IN RENAL OUTCOMES IN HYPERTENSIVE NEPHROSCLEROSIS

Practical point: African Americans with hypertension are at high risk of renal dysfunction. Obviously, do not wait for renal dysfunction to be established before beginning effective anti-hypertension therapy. We should protect the kidney as well as the heart and brain. Identifying and treating patients at the stage of microalbuminuria (20 to 200 mg/d) would lead to greater benefit than waiting for renal dysfunction to become established. Angiotensin converting enzyme inhibitors are the drugs of choice.

7-9 ANALGESIC USE AND RENAL FUNCTION IN MEN

This provides reassurance that there is not a strong relationship between chronic (up to 4 years) moderate use of acetaminophen, aspirin, and other NSAIDs and development of renal disease in persons with normal renal function.

This does *not* provide reassurance among those with initial renal dysfunction. NSAIDs in these patients may lead to further kidney dysfunction.

Primary care clinicians must remember that NSAIDs can have a deleterious effect on patients with heart failure and hypertension through their pharmacological effect on the kidney.

7-4 ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND PROGRESSION OF NON-DIABETIC RENAL DISEASE: Meta-analysis of Patient-Level Data

Antihypertension regimens which include ACE inhibitors are more beneficial in slowing the progression of non-diabetic renal disease than regimens that do not contain ACE.

Practical point: Chronic renal insufficiency is under-diagnosed and under-treated. Opportunities for prevention are lost. The presence of proteinuria in chronic renal disease is a strong indication for treatment with ACE. ACE inhibitors should be the antihypertensive agents of first choice in nondiabetic renal disease as well as in diabetic renal disease.

7-5 PATIENT-INITIATED TREATMENT OF UNCOMPLICATED RECURRENT URINARY TRACT INFECTIONS IN YOUNG WOMEN

Motivated and adherent young women can accurately self-diagnose and self-treat recurrent UTIs.

Practical point: Primary care clinicians should make this option available to select patients.

9-9 THE EFFECT OF IRBESARTAN ON THE DEVELOPMENT OF DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES.

In patients with type 2 diabetes, microalbuminuria, and hypertension, the angiotensin II blocker, irbesartan, was renoprotective, independent of its blood pressure lowering effect

Choice of an ACE inhibitor vs an angiotensin II blocker would depend on adverse effects (eg, cough) and cost.

Practical point: All patients with diabetes should be tested for microalbuminuria. Treatment with an ACE inhibitor or an angiotensin blocking drug should be started early.

9-19 SPIRONOLACTONE IN ADDITION TO ACE INHIBITION TO REDUCE PROTEINURIA IN PATIENTS WITH CHRONIC RENAL DISEASE

The study entered eight patients with various renal diseases and persistent proteinuria despite treatment with enalapril (*Vasotec*) for 12 months. Spironolactone 25 mg daily was then added.

After treatment, there was a mean 54% reduction in protein excretion. There was no significant reduction in BP or creatinine clearance.

"Spironolactone therapy may be useful in patients with proteinuria and renal impairment who still have proteinuria after treatment with ACE inhibitors."

Practical point: Spirinolactone add-on may be helpful in some patients with renal disease as well as in some with heart failure.

RESPIRATORY SYNCYTIAL VIRUS

10-12 CONTRIBUTION OF INFLUENZA AND RESPIRATORY SYNCYTIAL VIRUS TO COMMUNITY CASES OF INFLUENZA-LIKE ILLNESS

In individuals with influenza-like illness, there is a substantial potential for confusion between illness caused by RSV and IV. In this study about 20% of adults with flu-like symptoms were positive for respiratory syncytial virus. RSV is an important pathogen contributing to the burden of illness in the entire community in winter.

Practical point: Watch for development of RSV vaccine for adults.

RHEUMATIC FEVER

6-15 TIME TO TAKE SOUNDINGS IN ACUTE RHEUMATIC FEVER.

Doppler echocardiographic demonstration of subclinical carditis represents definite heart disease. The criteria for confirmation require that the regurgitant jet must extend 1 cm back of the valve and be holosystolic (mitral) and holodiastolic (aortic).

Practical point: Although rheumatic fever is rare in the US, it still occurs. Primary care clinicians should be aware that echocardiography may be a valuable aid in early diagnosis and lead to more effective prophylaxis.

SEASONAL AFFECTIVE DISORDER (SAD)

12-14 HELP ARRIVES WITH THE DAWN?

A recent investigation compared 30 minutes of bright light at 0600 hours against placebo and against dawn stimulation. Dawn stimulation consisted of exposure to white light of gradually increasing brightness which started at 0430 h while the patient was asleep. Brightness peaked at 250 lux in 90 minutes. Placebo consisted of dim red light. Dawn stimulation was associated with a significantly higher rate of remission. and a greater reduction in symptoms than either bright light or placebo. Part of the benefit may have been due to the method of delivery which helped patients adhere to a waking time of 0600 h, and thus a regular sleep schedule.

Practical point: Interesting. watch for further reports.

SIGMOIDOSCOPY

8-9 ONE-TIME SCREENING FOR COLORECTAL CANCER WITH COMBINED FECAL OCCULT-BLOOD TESTING AND EXAMINATION OF THE DISTAL COLON

One-time screening of asymptomatic subjects with FBOT plus sigmoidoscopy failed to identify about 1 of every 4 subjects with advanced neoplasia.

Practical point: Primary care clinicians should advise all patients over 50 to undergo periodic colonoscopy and omit FBOT and sigmoidoscopy.

SINUSITIS

12-5 COMPARISON OF CEFUROXIME WITH AND WITHOUT FLUTICASONE FOR THE TREATMENT OF RHINOSINUSITIS

The addition of fluticasone to xylometazoline and cefuroxime improved clinical success rates and accelerated recovery of patients with a history of chronic recurrent sinusitis who presented with acute sinusitis.

Practical point: Added fluticasone may be a possible benefit in a few patients.

SLEEP

11-8 PYRAZOLOPYRIMIDINES

Zaleplon (*Sonata*) has many attributes of the ideal hypnotic agent — rapid absorption, rapid onset, adequate duration of action, minimum or no residual effect on daytime performance, and no evidence of pharmacological tolerance or withdrawal. "It provides another very helpful option in the management of patients with insomnia."

SMOKING

5-14 MENINGOCOCCAL DISEASE

A review. Smoking and inhaling smoke may predispose to meningococcemia.

Practical point: Primary care clinicians should be prepared to administer antibiotics empirically to sick patients suspected of meningococcemia. Delay increases mortality.

6-14 SMOKING CESSATION AND THE COURSE OF MAJOR DEPRESSION

Smokers with a history of depression who abstained from smoking were at high risk of developing a new episode of major depression.

Practical point: How should primary care clinicians respond to this information? Which is worse -- continuing smoking or developing another episode of major depression? Is cigarette smoking always bad? Obviously, millions of persons choose to smoke fully knowing the risks. There must be some benefit. Relentlessly pushing some patients to stop smoking could drive them away. A frank discussion about pros and cons might lead to a trial of nicotine replacement.

7-11 ACUTE EFFECTS OF PASSIVE SMOKING ON THE CORONARY CIRCULATION IN HEALTHY YOUNG ADULTS.

Passive smoking substantially reduced coronary blood flow reserve in healthy non-smokers. Passive smoking may cause endothelial dysfunction in the coronary circulation in non-smokers.

This should convince the diehards who still maintain that harms of passive smoking are not proven. It strengthens the resolve of those who oppose smoking in public places

STATIN DRUGS (See also LIPIDS)

1-9 EARLY STATIN TREATMENT FOLLOWING MYOCARDIAL INFARCTION AND 1-YEAR SURVIVAL.

Early initiation of statin treatment in patients with acute MI was associated with reduced 1-year mortality. "Initiation of statin treatment before or at the time of hospital discharge should be recommended for all acute MI survivors with total cholesterol or low density cholesterol levels above current guideline levels for statin treatment as secondary prevention."

4-7 EFFECTS OF ATORVASTATIN ON EARLY RECURRENT ISCHEMIC EVENTS IN ACUTE CORONARY SYNDROMES: The MIRACL Study

High dose atorvastatin started within 1 to 3 days after presentation for acute coronary syndromes was associated with a reduction in risk of early recurrent ischemic events, but with no other significant clinical benefit.

Practical point: Statin drugs given immediately after onset of acute myocardial infarction or unstable angina may be associated with only small benefits over 4 months. Nevertheless, statins should be started for secondary prevention and maintained over years. Starting early in the hospital will encourage compliance.

4-8 EFFECT OF LIPID-LOWERING THERAPY ON EARLY MORTALITY AFTER ACUTE CORONARY SYNDROMES.

Prescription of a lipid-controlling drug at hospital discharge for patients with unstable angina or MI, was independently associated with reduced short-term mortality over 1 month and 6 months.

Practical point: There is good reason for prescribing statin drugs to patients with acute coronary syndromes (ie, established coronary disease) during their hospitalization or at discharge.

5-8 BENEFITS OF PRAVASTATIN ON CARDIOVASCULAR EVENTS AND MORTALITY IN OLDER PATIENTS WITH CORONARY HEART DISEASE ARE EQUAL TO OR EXCEED THOSE SEEN IN YOUNGER PATIENTS: The LIPID Trial

Practical point: Older persons with established coronary disease and average or moderately elevated cholesterol levels may benefit from secondary prevention with pravastatin therapy. Co-morbidity, expected length of life, and personal preference are contraindications, not age.

5-1 EXECUTIVE SUMMARY OF THE THIRD REPORT OF THE NATIONAL CHOLESTEROL EDUCATION PROGRAM (NCEP) EXPERT PANEL ON DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD CHOLESTEROL IN ADULTS (Adult Treatment Panel III)

Practical point: All primary care clinicians should have a copy of these guidelines available for reference and distribution to patients with lipid problems. This will include millions.

8-8 RISK OF MACULAR DEGENERATION IN USERS OF STATINS

An exciting, but preliminary report of considerable lowering of risk of macular degeneration in older persons taking statin drugs.

11-6 SIMVASTATIN AND NIACIN, ANTIOXIDANT VITAMINS, OR THE COMBINATION FOR THE PREVENTION OF CORONARY DISEASE.

Compared with placebo, combined niacin-statin (simvastatin) provided marked clinical and angiographic benefits in patients with established coronary disease and low HDL levels. (Secondary prevention). The decrease in LDL related to combined statin-niacin was greater than the average decrease reported from statin therapy alone. The increase in HDL was much more than usually reported from statins alone. The rate of major clinical events was reduced by 90% in the simvastatin + niacin group.

Antioxidants did not benefit. "Unless more compelling evidence appears, we see little justification for the use of antioxidant vitamins for the prevention of cardiovascular events."

STEATOHEPATITIS

9-14 METFORMIN IN NON-ALCOHOLIC STEATOHEPATITIS

In patients with steatohepatitis, metformin given over 4 months reduced ALT, increased insulin sensitivity, and decreased liver size.

Practical point: Primary care clinicians will encounter patients with steatohepatitis. Most will be secondary to alcoholism, obesity, or diabetes. Metformin may benefit a subset.

STROKE

1-6 ANTIHYPERTENSIVE DRUG THERAPIES AND RISK OF ISCHEMIC STROKE.

The study suggests a particular benefit of thiazide diuretics in reducing the risk of ischemic stroke.

Compared with those using beta-blockers alone, calcium blockers alone, or ACE inhibitors alone, users of a thiazide diuretic alone experienced a much lower incidence of ischemic stroke.

Among users of 2 drugs, those patients who received 2 drugs other than a thiazide had a 1.3 greater relative risk than those receiving a thiazide as one of the two.

The most recent (1997) report of the National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends diuretics as a first-line antihypertension agent.

1-17 INTAKE OF FISH AND OMEGA-3 FATTY ACIDS AND RISK OF STROKE IN WOMEN

Higher consumption of fish and omega-3 polyunsaturated fatty acids was associated with a reduced risk of thrombotic infarction, primarily among women who did not take aspirin regularly. No relation to hemorrhagic stroke.

Among users of 2 drugs, those patients who received 2 drugs other than a thiazide had a 1.3 greater relative risk than those receiving a thiazide as one of the two.

The most recent (1997) report of the National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends diuretics as a first-line antihypertension agent.

4-10 RISK, CAUSES, AND PREVENTION OF ISCHAEMIC STROKE IN ELDERLY PATIENTS WITH SYMPTOMATIC INTERNAL-CAROTID STENOSIS.

"If elderly people are denied therapy for reasons of prejudice and not of science, they may justifiably feel that they have been abandoned on the basis of age alone."

In the secondary prevention (after TIA or non-disabling stroke) of ipsilateral stroke, patients over age 75 with 50-99% symptomatic stenosis, benefited more from endarterectomy than younger patients.

And much more than those in the group receiving medical treatment alone.

Practical point: Elderly patients who have experienced a TIA or non-disabling stroke are at extremely high risk of a second stroke. Since the elderly live now live longer than in the past, in patients over age 75 the benefits of surgery may outweigh the risks of surgery and of continued medical treatment. They should be informed about the local experience of endarterectomy and given the opportunity to choose for themselves.

6-18 HIGH-DENSITY LIPOPROTEIN CHOLESTEROL AND ISCHEMIC STROKE IN THE ELDERLY: The Northern Manhattan Stroke Study

Increased HDL-c levels were associated with reduced risk of ischemic stroke in the elderly. This is possibly another benefit of statin drugs which raise HDL-c.

Practical point: Primary care clinicians should consider the entire lipid profile, not just the total cholesterol or the LDL-cholesterol, when advising patients about risks.

9-8 RANDOMIZED TRIAL OF A PERINDOPRIL-BASED BLOOD-PRESSURE-LOWERING REGIMEN AMONG 6105 INDIVIDUALS WITH PREVIOUS STROKE OR TRANSIENT ISCHAEMIC ATTACK.

In patients with previous stroke or TIA, a combination of an ACE inhibitor and a diuretic lowered mean BP from about 148/86 to about 125/75 and resulted in a large reduction in risk of recurrence of stroke.

"Treatment . . . should be considered routinely for patients with a history of stroke or TIA, irrespective of their BP."

Importantly, benefit for BP lowering was evident in patients not usually considered to be hypertensive — ie, those with "high normal" BP in whom BP was lowered from a mean of 136/79 to 127/75.

Practical point: A reduction to about 125/75 would benefit without causing harm.

9-12 TINZAPARIN IN ACUTE ISCHEMIC STROKE (TAIST): A Randomized, Aspirin-controlled Trial

Treatment with the low-molecular weight heparin, tinzaparin, within 48 hours of acute ischemic stroke did not improve functional outcome compared with aspirin. It was associated with increased intracerebral hemorrhage.

Practical point: Rely on aspirin alone

9-15 EFFECT OF LEVODOPA IN COMBINATION WITH PHYSIOTHERAPY ON FUNCTIONAL MOTOR RECOVERY AFTER STROKE

The brain is plastic. It is pliable and capable of being reformed. Specific transmitters are involved. Enhancement of functional motor recovery seems to rely on an increased concentration of norepinephrine at the synapses.

Levodopa is converted to dopamine in the brain. Small amounts are then converted to norepinephrine. Combined with physiotherapy, levodopa was an effective and safe method for improving motor recovery after stroke. In view of its minimal side effects, it will be a possible add-on during stroke rehabilitation.

Practical point: None at this time. I abstracted this study because it is so provocative. Watch for follow-ups.

11-12 A COMPARISON OF WARFARIN AND ASPIRIN FOR THE PREVENTION OF RECURRENT ISCHEMIC STROKE.

Over a 2 year period, there was no difference between aspirin and warfarin in prevention of recurrent non-cardiac stroke or death. For more than 50 years, physicians have prescribed warfarin for patients with non-cardioembolic stroke in the hope that subsequent strokes could be prevented. This treatment was based on a mixture of clinical experience, observational studies, and inferences about the pathophysiology of stroke.

"Aspirin alone, or in combination with some other antiplatelet agents appears to be a well-justified choice for the prevention of recurrent ischemic stroke"

Practical point: This simplifies secondary prevention.

SUBSTANCE ABUSE

4-18 TAKE HOME NALOXONE AND THE PREVENTION OF DEATHS FROM OPIATE OVERDOSE

Practical point: Naloxone, a rapidly acting opioid antagonist will save lives of the opioid abusers who overdose. It should be given routinely, on request, to all abusers.

We cannot abandon compassionate care of those who cannot or will not care for themselves.

TERMINAL CARE

4-15 UNDERSTANDING THE EXPERIENCE OF PAIN IN TERMINALLY ILL PATIENTS

Although half of terminally ill patients experience moderate to severe pain, only 30% of these wanted additional pain treatment. The number of patients experiencing pain remains too high, but the number is not as large as perceived.

Many patients are willing to tolerate pain for fear of addiction; dislike of mental or physical side effects; not wanting to take more pills or injections. Physicians must communicate more effectively that addiction to opioids given for pain relief is a myth.

Practical point: As usual, pain control as well as other aspects of treatment must be negotiated , and concordance reached, with each individual patient.

THROMBOLYTIC THERAPY (See also **MYOCARDIAL INFARCTION; STROKE**)

8-5 EFFICACY AND SAFETY OF TENECTEPLASE IN COMBINATION WITH ENOXAPARIN, ABCIXIMAB, OR UNFRACTIONATED HEPARIN: The ASSENT-3 Randomised Trial in Acute Myocardial Infarction

Tenecteplase is a new genetically engineered variant of alteplase (tPA; tissue plasminogen activator). It provides a new standard of fibrinolytic therapy by virtue of its equivalent efficacy with regard to 30-day mortality, its reduced propensity for bleeding complications, and its simple administration as a bolus.

“In view of the present data and the ease of administration, enoxaparin might be regarded an attractive alternative anticoagulant given in combination with tenecteplase.”

Taking into account efficacy and safety, the combination of full-dose bolus tenecteplase + enoxaparin for 7 days emerged as the best treatment in this trial. Because of ease of administration and the lack of monitoring of anticoagulation, this combination should be regarded as an attractive alternative pharmacological reperfusion strategy deserving further study.

Practical point: Primary care clinicians will soon have the opportunity and responsibility to apply immediate (bolus) out-of-hospital thrombolysis.

THYROID DISEASE

4-16 RISK OF FRACTURE IN WOMEN WITH LOW SERUM LEVELS OF THYROID-STIMULATING HORMONE

Older women with biochemical evidence of physiological hyperthyroidism (low TSH), mainly due to too high doses of exogenous thyroxine, but also due to endogenous "subclinical hyperthyroidism", had an increased risk of hip and vertebral fracture.

Practical point: Consider any woman with evidence of excess thyroid hormone production or administration at risk of increased severity of osteoporosis. Exogenous thyroxine dosage must be carefully monitored.

7-13 SUBCLINICAL HYPOTHYROIDISM

Routine screening, especially of older women, has been advocated, although not endorsed unanimously. The benefits of subsequent therapy have not been established in prospective trials. However, a decision and cost-effectiveness model calculated that screening women over age 35 every 5 years would be beneficial. Half the benefit would be from prevention of subsequent overt hypothyroidism, 30 percent for improved symptoms, and a smaller benefit from improvement in serum lipids.

Prevention of progression to overt hypothyroidism has been found to be about 4% per year in women with both an elevated TSH and antithyroid antibodies. (38 times that of women with normal values.) The NNT to prevent one patient from developing overt hypothyroidism = 4 to 14.

Practical point: Primary care clinicians must decide on long-term thyroxine supplementation or continued observation. I believe cautious supplementation is the best choice.

8-10 MANAGEMENT OF NODULAR THYROID DISEASE

Although the optimum diagnostic strategy for euthyroid patients with nodular thyroid disease is still a matter of debate, there is agreement that fine needle aspiration cytology and tests of thyroid function are cornerstones of investigation.

The challenge remains identifying which palpable nodules are malignant.

The advice regarding investigation of nodules to detect cancer differs from the old tradition in several ways:

1. Radionuclide scanning and ultrasound may not reliably differentiate malignant from benign nodules.
2. TSH suppression with thyroxine is not indicated.
3. Differentiating single and multinodular goiters is not helpful in assessing risk of cancer.
4. Overt thyroid dysfunction effectively rules out malignancy

8-15 SUBCLINICAL HYPERTHYROIDISM

"Subclinical hyper-thyroidism". (**SCHyperT**) is defined as — the combination of an *undetectable* serum thyrotropin concentration (**TSH**), as measured by an assay with a threshold of detection that is 0.1mU per liter or less, and *normal* serum thyroxine and triiodothyronine concentrations (usually at the upper end of the normal range).

For the many with endogenous SCHyperT who do not have multinodular goiter, and no complications from excess endogenous thyroxine production, treatment is not necessary. Thyroid function tests should be done every 6 months. Recognize that serum T3 may become elevated before T4.

Treatment of patients with SCHyperT due to nodular goiter is more routinely justified given the expected progression to overt hyperthyroidism. "It would be surprising if the complications of overt hyperthyroidism were not seen, albeit at a reduced frequency, in a condition that is effectively the mildest form of thyrotoxicosis."

Practical point: These patients should be followed for development of osteoporosis and atrial fibrillation.

ULTRASOUND

5-20 MICROBUBBLE CONTRAST AGENTS: A New Era in Ultrasound

Until recently, contrast agents had little place in ultrasonography. This has changed with the introduction of microbubbles— small (typically 3 um in diameter, gas filled bubbles that are usually given intravenously). Injecting a gas into the circulation may seem potentially hazardous, but extensive clinical experience has shown that the tiny volume of air or gas given (under 200 uL) is not dangerous.

Microbubbles work by resonating in an ultrasound beam, rapidly contracting and expanding in response to the pressure changes of the sound wave. They vibrate strongly at the high frequencies used for diagnostic ultrasound. This makes them several thousand times more reflective than normal body tissues.

Powerful applications are emerging.

URINARY TRACT INFECTION

6-13 RANDOMIZED TRIAL OF CRANBERRY-LIGONBERRY JUICE AND *LACTOBACILLUS* GG DRINK FOR THE PREVENTION OF URINARY TRACT INFECTION IN WOMEN.

Daily consumption of cranberry juice reduced the recurrence of urinary tract infections in young women. Lactobacillus did not.

Practical point: Primary care clinicians may suggest cranberry juice as a prophylactic measure in women with frequent recurrences

7-5 PATIENT-INITIATED TREATMENT OF UNCOMPLICATED RECURRENT URINARY TRACT INFECTIONS IN YOUNG WOMEN

Motivated and adherent young women can accurately self-diagnose and self-treat recurrent UTIs.

Practical point: Primary care clinicians should make this option available to select patients.

VASCULAR DEMENTIA

6-4 MIDLIFE VASCULAR RISK FACTORS AND ALZHEIMER'S DISEASE IN LATER LIFE

Raised systolic BP and high cholesterol concentrations (and particularly the combination) in midlife were associated with increased risk of Alzheimer's disease later in life. This possible added benefit would be most welcome.

Practical point: Both factors should be controlled in mid-life regardless of any possible benefit on reducing risk of Alzheimer's. Control of both to reduce risk of cardiovascular disease is one of the great challenges and opportunities for primary care clinicians. Any possible reduction in incidence of Alzheimer's would be an additional benefit. .

12-11 UNTANGLING VASCULAR DEMENTIA

Questions remain about the mechanism of the interaction between cerebrovascular disease and Alzheimer's in an individual patient. Alzheimer's disease cannot be ruled out by clinical investigation. A diagnosis of vascular dementia does not rule out Alzheimer's. The part that cerebrovascular disease may play in producing symptoms of dementia is particularly difficult to understand when it is accompanied by histological features of Alzheimer's disease.

"It is not surprising that accurate clinical diagnosis of Alzheimer's disease seems to be easier than vascular and mixed dementia. Meanwhile, it is worth noting that although 'pure' vascular dementia exists, vascular disease may be an important and potentially treatable contributor to Alzheimer's disease."

Practical point: We await untangling the pathogenesis of Alzheimer's, and have great hope for development of specific preventive measures for the disease. In the meantime, we can do a great deal to protect the vascular system of the brain. The same prophylactic measures apply to the brain as to the coronary circulation.

VENOUS THROMBOSIS-THROMBOEMBOLISM

5-13 ROUTINE HOME TREATMENT OF DEEP VEIN THROMBOSIS

A study in this issue of BMJ adds to the growing evidence supporting the safety and feasibility of home treatment for acute DVT. The investigators concluded that most outpatients presenting with acute DVT can be treated at home. Admission to hospital is required mainly due to infrastructure problems, rather than for medical reasons.

Practical point: Some primary care clinicians may be able to arrange home care. It requires adequate resources.

7-16 EXTENDED-DURATION PROPHYLAXIS AGAINST VENOUS THROMBOEMBOLISM AFTER TOTAL HIP OR KNEE REPLACEMENT

Among patients undergoing elective hip and knee replacement, outpatient LMW heparin continued for 4 to 6 weeks after discharge reduced the frequency of DVT.

Practical point: For the many patients for whom extended heparin or warfarin is not feasible, aspirin should be considered an option.

7-12 MANAGEMENT OF SUSPECTED DEEP VENOUS THROMBOSIS IN OUTPATIENTS USING CLINICAL ASSESSMENT AND D-DIMER TESTING

The combination of a low pretest probability of DVT and a negative D-dimer test rules out DVT.

Practical point: Primary care clinicians may use a D-dimer test to help *rule out* DVT in select low probability patients. D-dimer is not useful in *ruling in* DVT. It is not useful in patients with moderate or high probability of DVT.

7-17 THREE MONTHS VERSUS ONE YEAR OF ORAL ANTICOAGULANT THERAPY FOR IDIOPATHIC DEEP VENOUS THROMBOSIS.

In patients with acute idiopathic DVT, continuing anticoagulation for 1 year reduced recurrence during that year. However, after discontinuing anticoagulation, thrombosis recurred at a rate similar to the rate in those who discontinued after 3 months.

Practical point: Primary care clinicians face the decision – continue or discontinue anticoagulation? I believe the answer depends on the severity of the DVT, the preference of the patient, and the local availability of logistic support for anticoagulation. If discontinued, recurrence is likely. We should search for underlying thrombogenic factors in these patients. If the decision is made not to continue warfarin, these patients should be placed on continuous aspirin.

VITAMINS

12-3 WHAT VITAMINS SHOULD I BE TAKING, DOCTOR?

Standard advice in the past recommended that vitamin supplements were not needed for persons with an adequate diet. A sea change has occurred. Multivitamin supplements are recommended.

The commentators cite evidence for benefits of folic acid, vitamin B6, vitamin B12, Vitamin D, and vitamin E.

Practical point: Many primary care clinicians now recommend routine use of supplements.

WEBSITES

4-19 ANTIBIOTIC DATABASE LAUNCHED

Johns Hopkins has a free to all peer reviewed database presenting the latest information on antibiotics and infectious diseases. (www.hopkins-abxguide.org).

Practical point: This easily accessed website should be most helpful to primary care clinicians.

4-20 A NEW WEB SITE AND A NEW POLICY

The NEJM's web site has been changed from www.nejm.com to www.nejm.org. An improved search system makes it possible to search the full text of all NEJM articles as far back as 1993.

Beginning six months after publication, the full text of all original articles and special articles will be available on line *free of charge*.

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